Postgraduate Medicine

Volume 29 · Number 2

FEBRUARY · 1961

OFFICIAL JOURNAL OF THE INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

TABLE *of* CONTENTS

Nutrition in Relation to Arteriosclerosis
FREDRICK J. STARE, M.D. 133

Appraisal of Needle Biopsy
RAYMOND BANGLE, JR., M.D. 138

Uterine Bleeding in the Second Trimester Caused by Abnormal Placental Development
J. EDWARD HALL, M.D. 147

Surgical Considerations of Aneurysms and Atherosclerotic Occlusive Lesions of the Aorta and Major Arteries
E. STANLEY CRAWFORD, M.D., MICHAEL E. DEBAKEY, M.D., DENTON A. COOLEY, M.D. AND GEORGE C. MORRIS, JR., M.D. 151

The Subcuticular Suture
RICHARD E. STRAITH, M.D., JAMES M. LAWSON, M.D. AND C. JACK HIPPS, M.D. 164

PSYCHOSOMATIC MEDICINE—SPECIAL SERIES

When Do You Refer a Child to a Psychiatrist?
HARRIS E. KAROWE, M.D. 174

NUTRITION IN CLINICAL MEDICINE

The Influence of Chronic Undernutrition on Bone Growth in Children
SAMUEL DREIZEN, D.D.S., M.D., ROBERT E. STONE, M.D. AND TOM D. SPIES, M.D. 182

CLINICAL STUDY

1-Phenethylbiguanide—an Orally Administered Hypoglycemic Agent
STANLEY S. BERGEN, JR., M.D. AND WILLIAM S. NORTON, II, M.D. 194

(Continued on page A-4)

Postgraduate Medicine is published monthly at Minneapolis, Minn., by IPMA Publishing Co., G. Victor Lowrie, executive vice-president; William H. Hull, professional relations manager; Muriel D. Ries, circulation manager; Fred Couzens, Eastern manager, 420 Lexington Ave., New York 17, N.Y., telephone Murray Hill 4-7752; Arthur G. Sullivan, Jr., Central-West manager, 203 North Cedar Street, Horicon, Wis., telephone Hunter 5-2003. Advertising representatives: McDonald-Thompson, 1008 Western Ave., Seattle 1, Wash.; 625 Market St., San Francisco 5, Calif.; 3727 W. 6th St., Los Angeles 5, Calif.; 2727 Oak Lane Ave., Dallas 19, Tex.; 3217 Montrose Blvd., Houston 6, Tex.; 620 Sherman St., Denver 3, Colo. Publication date: 10th of the month. Subscription rate $10.00 a year in the United States and Canada; $12.00 in foreign countries. Two volumes a year. Address all editorial and business correspondence to **Postgraduate Medicine**, Essex Building, Minneapolis 3, Minn., telephone Federal 9-8836.

© 1961 by IPMA Publishing Co. Title Reg. U. S. Pat. Off.
Second-class postage paid at Minneapolis, Minnesota and at additional mailing offices. Printed in U.S.A.

SCIENTIFIC EXHIBIT

Emergency Care of the Eye
LEO L. MAYER, M.D. 199

CLINICOPATHOLOGIC CONFERENCE

Case Report
FROM THE VETERANS ADMINISTRATION HOSPITAL, HINES, ILLINOIS 209

ART IN THE TEACHING OF MEDICINE—SPECIAL SERIES

The Physician in the Caricature
HELMUTH NATHAN, M.D., JOSEPH HIRSH, M.D. AND
NESRIN BINGOL, M.D. 214

SELF-HELP DEVICES

Selection of Wheel Chairs: Consideration of Specific Disabilities
EDWARD W. LOWMAN, M.D. AND HOWARD A. RUSK, M.D. 219

POSTGRADUATE CLINICAL NOTES

154. Enzyme Deficiencies 163
155. The Brain 181

DEPARTMENTS

EDITORIALS 224
Palliative or Nonpalliative: A Surgical Problem
The Peril of Delay in Publishing
Witnesses in Forensic Medicine
Strange Words

FORTHCOMING FEATURES A-9

YOUR QUESTIONS ANSWERED A-18
Pulmonary Fibrosis
"Glitter Cells"
Hodgkin's Disease
Encopresis

LABORATORY NOTES A-26
The Albumin-Globulin Ratio
ELLIS S. BENSON, M.D.

WHAT'S HAPPENING IN MEDICINE ..... Facing A-32-33

FORENSIC MEDICINE A-40
The Cardiac: Industry's Medicolegal Problem
OLIVER C. SCHROEDER, JR., LL.B.

(Continued on page A-6)

What does high "ABA" mean to you?

High serum levels of antibacterial activity mean fewer treatment failures in severe infections or in infections only marginally sensitive to penicillin. In other words, high "ABA" means . . .

consistently dependable clinical results

V-CILLIN K®

(penicillin V potassium, Lilly)

intense antibacterial activity

V-Cillin K produces greater antibacterial activity in the serum against the common pathogens than any other oral penicillin.[1-3]

unsurpassed safety

No form of penicillin has been shown to be less allergenic or less toxic than V-Cillin K.[4,5]

proved clinical effectiveness

Documented experience with penicillin V and potassium penicillin V reveals the clinical excellence of V-Cillin K.

Eli Lilly and Company
Indianapolis 6, Indiana, U.S.A.

133216

Now at lower cost to your patient

Prescribe V-Cillin K, in scored tablets of 125 and 250 mg., or V-Cillin K, Pediatric, in 40 and 80-cc. bottles.

References

1. McCarthy, C. G., and Finland, M.: Absorption and Excretion of Four Penicillins, New England J. Med., *263*:315, 1960. 2. McCarthy, C. G., Hirsch, H. A., and Finland, M.: Serum Levels after Single Oral Doses of 6-(α-phenoxypropionamido) Penicillanate and Penicillin V, Proc. Soc. Exper. Biol. & Med., *103*:177, 1960. 3. Griffith, R. S.: Comparison of Antibiotic Activity in Sera after the Administration of Three Different Penicillins, Antibiotic Med. & Clin. Therapy, *7*:129, 1960. 4. Editorial: New England J. Med., *263*: 361, 1960. 5. Editorial: New York J. Med., *60*:498, 1960.

MEETINGS AND POSTGRADUATE COURSES A-50, 146

RADIOLOGY FOR PRACTICING PHYSICIANS A-59
Intensification of the Fluoroscopic Screen
RUSSELL H. MORGAN, M.D.

MEDICINE FROM ABROAD A-76

NEWS OF INTERSTATE A-94

NEW FOR YOUR ARMAMENTARIUM A-100

PRODUCTS BY THERAPY INDICATIONS A-108

YOUR FINANCES
Financial Planning for the Medical Practitioner A-115

THE MEDICAL BOOKMAN A-138

GREAT NAMES IN AMERICAN MEDICAL HISTORY A-160
William Crawford Gorgas, M.D., Alabama

DR. PEPYS' PAGES. Morris Fishbein, M.D. A-166

THE MEDICAL MUSE. Richard Armour A-169

INDEX TO TECHNICAL EXHIBITS A-176

Information for AUTHORS

The Editors of POSTGRADUATE MEDICINE will be pleased to consider original papers in the fields of general medicine, as well as all the specialties, so presented as to be of value and interest to practicing physicians.

Papers should be typewritten, double spaced, and the original, not a carbon copy, should be submitted. Tissue weight paper should not be used. It is suggested that manuscripts comprise a maximum of approximately 3000 words. Authors' full names, academic or professional titles, and complete addresses should be given.

Bibliographies should be kept to a minimum and typed on separate sheets. References should include the author's full name, complete title of article, abbreviated name of journal, volume number, first page and year. References to books, monographs and pamphlets should include the author, title, name and city of the publisher, year of publication, edition and page number of the reference. References should be numbered consecutively throughout the paper and listed in order by number from the text.

POSTGRADUATE MEDICINE stresses the use of appropriate illustrative material suitable for good reproduction. All costs for black and white reproduction are routinely assumed by The Journal. Illustrations should be identified by number and author's name and the top indicated. They must be accompanied by legends numbered to correspond and the position in the text indicated.

Galley proofs are furnished authors in advance of publication. Reprints are available and a price list and order form are submitted with the galley proofs.

All correspondence pertaining to editorial matters should be addressed to the Editorial Department, POSTGRADUATE MEDICINE, Essex Building, Minneapolis 3, Minnesota.

SAUNDERS BOOKS

Just Ready!

1961 Current Therapy

Today's Best Treatments

You'll find here the surest, most effective treatments currently known to medical science for virtually every disease you are likely to meet. 314 contributors tell you in clear, concise language exactly how they proceed in treating these disorders. Over 80% of the articles in the 1961 volume are changed in a significant manner. New subjects include: cardiac arrest; the chronic leukemias; pseudomembranous enterocolitis; varicosities in pregnancy; poison control centers in the United States and Canada.

Among the 248 completely rewritten articles are: the common cold; diphtheria; food poisoning; intestinal parasitism; meningitis; poliomyelitis; rheumatic fever; congestive heart failure; hypertension; acute myocardial infarction; parenteral fluid therapy in children; tumors of the stomach; occupational dermatoses; cerebral vascular accidents; neurosis; bursitis subacromial; tumors of the brain; bleeding in late pregnancy and early puerperium.

By *314 Outstanding Authorities* selected by a *Special Board of Consultants*. Edited by HOWARD F. CONN, M.D. 806 pages, 8¼" x 11". $12.50. *New!*

Edwards—An Atlas of Acquired Diseases of the Heart and Great Vessels

In 3-Volumes—Ready March!

Anyone concerned with heart disease will find this magnificent new 3-volume atlas invaluable. It is today's most complete and meaningful presentation of structural changes in acquired heart disease, and the manner in which these morphological alterations influence function. Its wide coverage ranges from rheumatic carditis and hypertension to myocardopathies and atherosclerosis of the aorta. Dr. Edwards covers both major and less common lesions with brilliantly clear illustrations of gross anatomy and histologic changes. For major disease entities he also presents anatomic representations of functional derangements, differential diagnosis, clinical features and complications. Over two thousand illustrations include illuminating radiograms and electrocardiograms, as well as clear photographs of dissected hearts.

By JESSE E. EDWARDS, M.D., Consultant, Section of Pathologic Anatomy, Mayo Clinic, and Professor of Pathology, Mayo Foundation, Graduate School, University of Minnesota, Rochester. With the Assistance of HENRY N. NEUFIELD, RAYMOND D. PRUITT, ROBERT PARKER, and HOWARD B. BURCHELL. Three volumes, totalling about 1450 pages, 8" x 11¼", with 2333 illustrations. About $65.00. *New—Ready March!*

—ORDER TODAY!— PGM 2-61

W. B. **SAUNDERS** Company, West Washington Square, Philadelphia 5

Please send and charge my account

☐ *1961 Current Therapy* *$12.50*

☐ *Edwards Atlas of Acquired Diseases of the Heart* ..... *About $65.00*

Name .....

Address .....

Your Questions answered

Readers may send questions from their own practice or other medical problems which will be answered by qualified consultants. Replies are forwarded by mail immediately and selected questions and answers are published each month in this section.

• PULMONARY FIBROSIS

Q. I am treating a man who has pulmonary sclerosis with triamcinolone (KENACORT®) and other medicaments, including iodine. What further therapy is indicated?

M.D.—Peru

A. The diagnosis of pulmonary sclerosis has been interpreted as synonymous with diffuse interstitial pulmonary fibrosis of indeterminate origin. If the severity or course of this disease indicates the need for treatment, the use of steroids represents the only therapy which has any rationale except for supportive measures such as the giving of oxygen and similar procedures.

The initial dose of steroids employed varies; however, a total daily dosage equal to eight times the standard replacement dosage is usually adequate. This amount is gradually decreased, and, if there is no abatement of symptoms or if objective measurements of pulmonary function do not reflect improvement, steroid therapy should be discontinued. If improvement is noted, treatment should be extended for at least a year and sometimes indefinitely. The maintenance dosage during most of this time should be the smallest which will sustain whatever improvement the patient has shown.

If the patient is sensitive to tuberculin, 300 mg. isoniazid should be given daily as prophylactic treatment for the possible reactivation of pulmonary tuberculosis during the administration of steroids. No other specific medicaments are of value, except those indicated by specific symptoms.

Arrival at a diagnosis of diffuse interstitial pulmonary fibrosis should follow the exclusion of systemic illnesses which may be associated with a picture of pulmonary fibrosis, occupational diseases associated with pulmonary fibrosis, sarcoidosis, and exposure to inhalants known to produce a picture of pulmonary fibrosis. Biopsy of nodes in the scalenus area and of tissue from the lungs also should be considered.

The term "pulmonary sclerosis" also might have reference to primary pulmonary hypertension. Ordinarily, steroids would not be administered for this condition.

• "GLITTER CELLS"

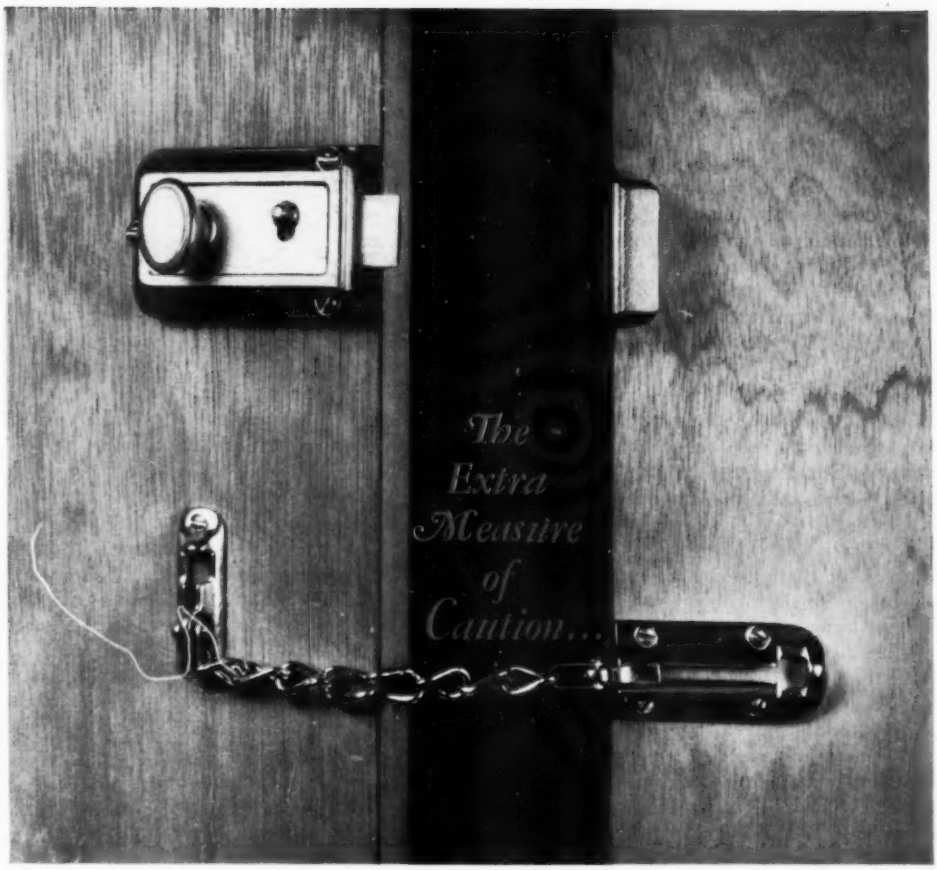
Q. What is the significance of glitter cells in chronic pyelonephritis? Are there any specific references to this subject in the literature?

M.D.—Wisconsin

A. The glitter cell is a pale-staining leukocyte containing cytoplasmic granules which exhibit Brownian movement. This type of leukocyte is found in largest numbers in the urinary sediment of patients who have intrarenal inflammation.

References pertaining to glitter cells include the following: (1) Sternheimer, R. and Malbin, B. I.: New stain for urinary sediment: Its value in the differential diagnosis of hypertension. Am. Heart J. 37:678-679 (April 1) 1949; (2) Berman, L. B., Screiner, G. E. and Feys, J. O.: Observations on the glitter-cell phenomenon. New England J. Med. 255:989-991 (November 22) 1956; and (3) Poirier, K. P. and Jackson, G. E.: Characteristics of leukocytes in the urine sediment in pyelonephritis: Correlation with renal biopsies. Am. J. Med. 23:579-586, 1957.

(Continued on page A-20)



Tetracycline now combined with the new, more active antifungal antibiotic – Fungizone – for broad spectrum therapy / antimonilial prophylaxis

A new advance in broad spectrum antibiotic therapy, MYSTECLIN-F provides all the well-known benefits of tetracycline and also contains the new, clinically proved antifungal antibiotic, Fungizone. This Squibb-developed antibiotic, which is unusually free of side effects on oral administration when given in oral prophylactic doses, has substantially greater in vitro activity than nystatin against strains of Candida (Monilia) albicans.

Thus, in addition to providing highly effective broad spectrum therapy, MYSTECLIN-F prevents the monilial overgrowth in the gastrointestinal tract so commonly associated with such therapy. It helps to protect the patient from troublesome, even serious, monilial complications.

New Mysteclin-F provides this added antifungal protection at little increased cost to your patients over ordinary tetracycline preparations.

Available as: MYSTECLIN-F CAPSULES (250 mg./50 mg.) MYSTECLIN-F HALF STRENGTH CAPSULES (125 mg./25 mg.) MYSTECLIN-F FOR SYRUP (125 mg./25 mg. per 5 cc.) MYSTECLIN-F FOR AQUEOUS DROPS (100 mg./20 mg. per cc.)

For complete information, consult package insert or write to Professional Service Department, Squibb, 745 Fifth Avenue, N. Y. 22, N. Y.

NEW

MYSTECLIN-F

Squibb Phosphate-Potentiated Tetracycline (SUMYCIN) *plus* Amphotericin B (FUNGIZONE®)

SQUIBB *Squibb Quality – the Priceless Ingredient*

'MYSTECLIN'®, 'SUMYCIN'® AND 'FUNGIZONE'® ARE SQUIBB TRADEMARKS

• HODGKIN'S DISEASE

Q. A 33 year old woman with a large mass in the right groin, multiple nodes in the right axilla, and cervical pain was first seen in December 1958. Biopsy of an axillary lesion revealed Hodgkin's disease. Other examinations, including x-rays of the chest and of the upper part of the gastrointestinal tract, barium enema studies, and intravenous pyelography, gave normal results.

The mass in the groin was treated with intravenously administered nitrogen mustard and with roentgen rays. The response was excellent, and the adenopathy disappeared. However, in May 1959 there was an exacerbation, with fever and reappearance of the nodes in the same area. A second course of nitrogen mustard produced an excellent remission. A third exacerbation occurred in November, with the adenopathy reappearing in the right axilla and groin. There was no hepatosplenomegaly, and the chest x-ray showed normal findings. A third course of nitrogen mustard produced a remission of about six weeks' duration. In February 1960 the patient was given 5 mg. triethylene melamine weekly for five weeks. The size of the nodes decreased, and her fever dropped. In April a large mass appeared in the left groin. It was surrounded by marked induration which caused lymphatic obstruction and painful edema of the left thigh. Roentgen therapy given daily for 10 days produced some remission.

The patient's only medical problem is chronic anemia associated with Hodgkin's disease. What further treatment do you suggest?

M.D.—Michigan

A. The possibility of prolonged remission in this case is poor, since the presence of fever and anemia indicates that the disease has caused systemic involvement as well as involvement of the lymph nodes. Generally, systemic involvement indicates extensive utilization of chemotherapy, even though it constitutes only a delaying action. However, in this case the fullest use should be made of radiotherapy, particularly if the function of the bone marrow has not been compromised severely by the disease or treatment. Since the para-aortic nodes also may be involved, if feasible, radiotherapy should be administered to the para-aortic areas as well as to the enlarged peripheral nodes.

The chemotherapeutic agent of choice is nitrogen mustard, which should be used in addition to radiotherapy when systemic symptoms are in preponderance over local lesions of the lymph nodes. The orally administered alkylating agent LEUKERAN® is sometimes used: it may produce more prolonged results, since it is given daily in a dose of 0.2 to 0.3 mg. per kilogram of body weight. A course of Leukeran usually consists of a total of 6 to 10 mg. per kilogram of body weight.

• ENCOPRESIS

Q. A five and one-half year old child has had a history of fecal incontinence since birth. There has been no loss of bladder control. The child is withdrawn and displays both clinging dependence and continuous resentment toward the mother. No overt neurologic symptoms are evident. What are your suggestions for evaluation and treatment?

M.D.—Pennsylvania

A. While the fecal incontinence is a normal characteristic of infants, persistence after two years of age is called encopresis (psychically caused involuntary defecation). The patient is nearly always a boy. In some children, faulty training may be a factor; others are too preoccupied to take time for normal evacuation. There also are some children who appear to derive satisfaction from embarrassing the parent, and still others may have neuromuscular disease.

Acquired megacolon is accompanied by fecal soiling and must be differentiated from Hirschsprung's disease (congenital megacolon) by proper x-ray study. If the stools are hard and the abdomen distended, megacolon should be ruled out. Soiling due to emotional disturbance has at times been associated with a domineering mother, maternal deprivation, or overambitious and precise parents. Occasionally, soiling reflects overconcern of the mother with the child's intestinal functions.

In the child in question, the behavior and attitudes described suggest an emotional disorder. If the cause is carelessness, discuss the social implications and encourage the parents to see that there is a regular and proper time for defecation each morning. If the stools are frequent and loose, a careful dietary regimen may help. If there is a serious psychologic problem, psychiatric help is indicated. Shaming is futile and only adds to the difficulty.

If you want an antimicrobial:

1. With outstanding effectiveness
2. With a remarkable safety record
3. That need be given only once a day
4. Which is "kind to the purse"

change to

MADRIBON

ROCHE

AS A SERVICE TO THE PRESCRIBING PHYSICIAN, BELOW IS A COMPLETE STATEMENT OF DOSAGE AND PRECAUTIONS AS SET FORTH IN THE BASIC PRODUCT LITERATURE.

DOSAGE (Tablets and Suspension)

For severe infections:

Adults: 4 tablets or 8 teaspoonfuls (2 Gm) initially followed by 2 tablets or 4 teaspoonfuls (1 Gm) daily thereafter.

Children:

Body Weight	Initial Dose	Daily Dose Every 24 Hours Thereafter
20 lbs	0.5 Gm { 1 tablet or { 2 teaspoonfuls	0.25 Gm { ½ tablet or { 1 teaspoonful
40 lbs	1 Gm { 2 tablets or { 4 teaspoonfuls	0.5 Gm { 1 tablet or { 2 teaspoonfuls
80 lbs	2 Gm { 4 tablets or { 8 teaspoonfuls	1 Gm { 2 tablets or { 4 teaspoonfuls

DOSAGE (Pediatric Drops)

For moderate to severe infections: 2 drops (25 mg) per pound body weight followed by 1 drop (12.5 mg) per pound body weight daily thereafter.

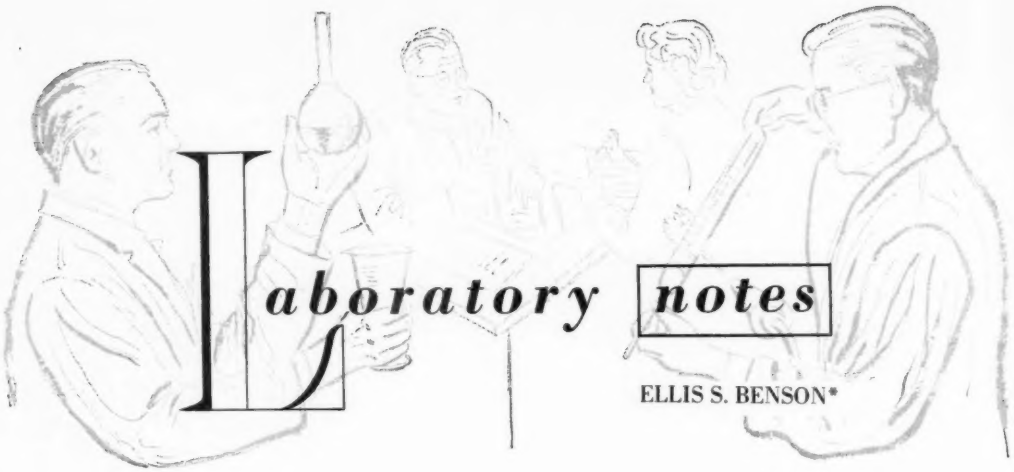
Continue therapy for 5 to 7 days or until patient is asymptomatic for at least 48 hours.

For mild infections: Less severe infections will usually respond to one-half the above dosage.

Caution: The usual precautions in sulfonamide therapy should be observed, including the maintenance of an adequate fluid intake. In the event of headache, nausea, vomiting, urticaria, rash, fever or hematuria, the use of the drug should be discontinued. When Madribon is used intermittently or for prolonged periods, blood counts should be performed to determine whether blood dyscrasias have occurred. The use of the drug should be stopped immediately if alterations in the hematopoietic system are observed. Patients with impaired renal function should be followed closely since renal impairment may cause excessive drug accumulation. Madribon should not be administered to patients with a history of adverse reactions to sulfonamide therapy.

Madribon, like most sulfonamides and certain other drugs, is probably contraindicated in premature infants — and newborn infants for the first week of life — because of underdeveloped enzyme systems and immature liver and renal functions.

Packages: Madribon Tablets: 0.5 Gm, double-scored, monogrammed, gold colored — bottles of 30, 100, 250, and 1000. Madribon Suspension: 0.25 Gm/teasp. (5 cc), custard flavored — bottles of 4 oz and 16 oz. Madribon Pediatric Drops: 250 mg/cc (20 drops) — 10-cc bottle with drop-dispensing tip.



Laboratory notes

ELLIS S. BENSON*

The Albumin-Globulin Ratio

THE ratio of serum albumin to serum globulin, commonly termed the A/G ratio, has had a hallowed place among the diagnostic criteria provided by the laboratory in the study of disease. The ratio is characteristically lowered or inverted in a number of disease processes, notably cirrhosis, hepatitis, nephrosis and multiple myeloma. In most of these instances, lowering of the ratio is due to both lowered serum albumin and increased serum globulin concentrations.

Much of the data in the literature concerning the A/G ratio in health and disease, until the past few years at least, were based on the use of the Howe[1] method of fractionation of serum albumin and globulin, which was introduced in 1921. This method depended on the addition of sodium sulfate solution to serum to obtain a final concentration of 21.5 per cent sodium sulfate. Globulin was thought to be precipitated at this concentration of salt, and the protein remaining in solution was considered to be albumin.

When Tiselius[2] introduced his method of electrophoresis to the study of plasma proteins in 1937, a number of workers attempted to compare the results of salt fractionation with those obtained by electrophoresis. It soon became apparent that the Howe method was inadequate for separating albumin and globulin.[3] Not all the globulin was precipitated from serum at a salt concentration of 21.5 per cent; some of it remained in solution with the albumin. Thus, albumin concentrations obtained by the Howe method were apparently too high and globulin concentrations were too low. The globulin remaining in solution was part of the alpha-globulin. Consequently, a serum with decreased albumin and increased alpha-globulin, such as that which might occur in nephrosis, could have a normal A/G ratio by the Howe method.

Rather than permit this situation to continue, certain investigators attempted to improve the chemical methods of fractionation in order to bring them more in line with the results obtained by electrophoresis. Majoor[4] and Milne[5] independently proposed fractionations based on the use of higher concentrations of sodium sulfate. The results obtained by

(Continued on page A-28)

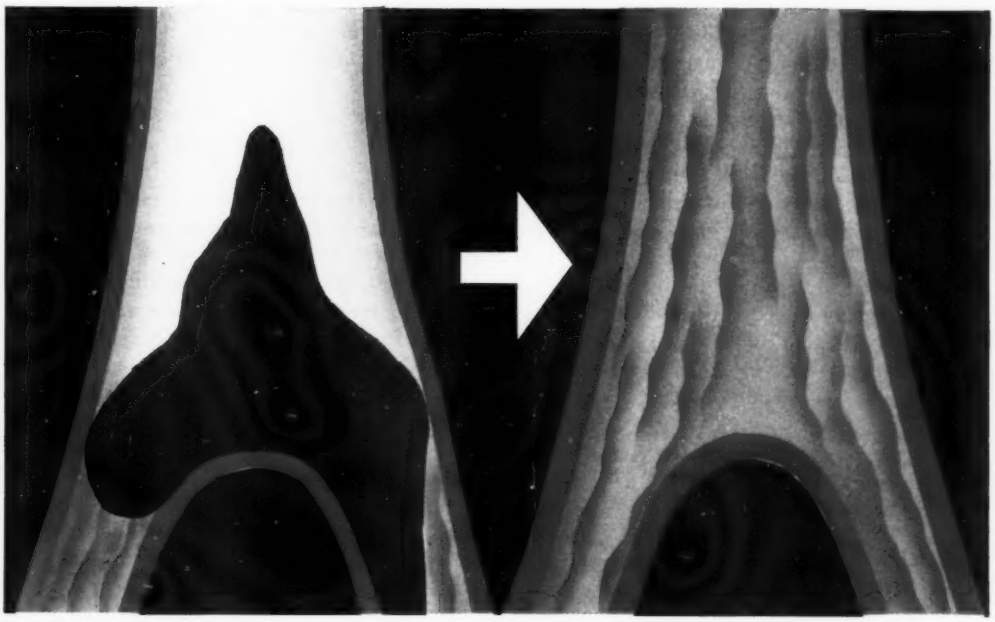
*Director of Hospital Laboratories and Associate Professor of Clinical Laboratory Medicine and of Pathology, University of Minnesota Medical School, Minneapolis, Minnesota.

clinical endorsement grows as proof accumulates

ACTASE
TRADEMARK

Fibrinolysin (Human)

NOT JUST A NEW DRUG... *A NEW THERAPY*



Ortho

SPECIFIC FOR THE DISSOLUTION
OF INTRAVASCULAR CLOTS

these methods agreed well with those obtained by electrophoresis, and thus these new methods gained approval as having more validity than the Howe method. A serious disadvantage, however, arose from the fact that the solutions of sodium sulfate used by Majoor and Milne were nearly saturated. Crystallization of the salt occurred at room temperature, making it necessary to store the solutions and to use them at 37° C. Even at this temperature, solutions are frequently unstable. This disadvantage has been overcome by substituting sodium sulfite, which has a solubility in water that is greater than that of sodium sulfate.

In Reinhold's[6] method, a mixture of sodium sulfate and sulfite is used, the solubilities being additive, and the final salt concentration is 26 per cent. We have used a modification of the method of Wolfson and Cohn and associates,[7] in which 28 per cent sodium sulfite is used. To 4.8 ml. of the salt solution is added 0.2 ml. of serum to give a final salt concentration of 26.9 per cent. In both of these methods, ether is then added, as originally proposed by Kingsley,[8] to make the precipitation of globulins more rapid at room temperature. In the Wolfson-Cohn method,[7] a mixture of ether and SPAN® 20,* a surface-active agent, is added to reduce the denaturization (and subsequent precipitation) of albumin by ether at the salt concentrations employed in these methods.

The method of fractionation which we use in our laboratory is a slightly modified version of the Wolfson-Cohn method and may be described briefly as follows:[9]

Reagents

1. 28 per cent sodium sulfite. Dissolve 280 gm. anhydrous sodium sulfite in 1 l. of water at 28° C. Store at 37° C.

2. Span-ether. To 1 ml. of Span 20, add 99 ml. of ethyl ether U.S.P. Shake to mix and filter rapidly into a 100 ml. volumetric flask. Dilute to volume with ether. Store in tightly stoppered bottle.

3. 0.9 per cent sodium chloride solution.

*Atlas Powder Co., Wilmington, Delaware.

4. Biuret reagent.
   9.0 gm. potassium sodium tartrate (Rochelle salt).
   3.0 gm. copper sulfate.
   5.0 gm. potassium iodide.
   0.2 N sodium hydroxide (carbonate-free).

Dissolve Rochelle salt in approximately 400 ml. of 0.2 N sodium hydroxide, to which the copper sulfate is added and dissolved by stirring. Dissolve the potassium iodide and dilute the solution to 1000 ml. with 0.2 N sodium hydroxide. Keep the solution in paraffin-lined or polyethylene bottles. This biuret reagent is essentially that of Weichselbaum.[10]

5. Protein standard: 1 ml. 6 per cent bovine albumin* diluted to 25 ml. with saline (0.9 per cent sodium chloride).

Procedure

Into a centrifuge tube, transfer by pipet 4.8 ml. of 28 per cent sodium sulfite. Add 0.20 ml. of serum. Mix by inversion, using a rubber stopper. Add 1 ml. of Span-ether, stopper, and mix by inverting gently but completely 12 times. Loosen rubber stopper and centrifuge 5 to 10 minutes at 1500 to 2000 rpm. The globulin will be packed at the ether-water interface; the albumin will remain in solution in the sulfite.

When the centrifuge tube is carefully tilted, the protein "button" will disengage itself from the side of the tube, permitting the withdrawal of a 3.0 ml. aliquot of the centrifugate. Transfer this aliquot to a colorimeter tube containing 2.0 ml. saline. Prepare a blank of 3 ml. of sulfite plus 2 ml. of saline.

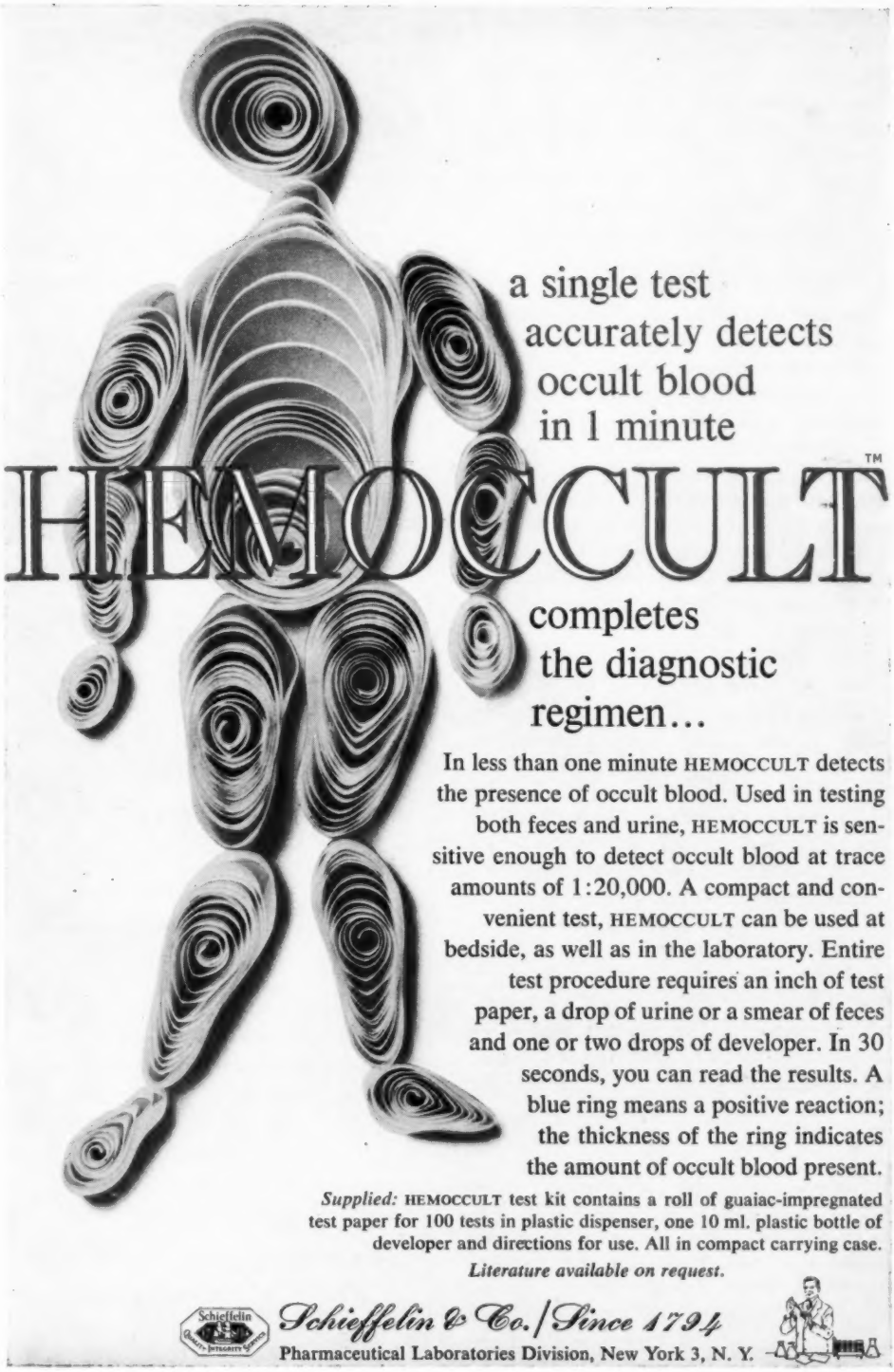
Because the salt concentration affects the slope of the biuret graph, albumin standards must be run at the same salt concentration as the serum samples.

Standards are prepared as follows: 3.0 ml. sulfite plus 1.0 ml. working protein standard plus 1.0 ml. saline, and 3.0 ml. sulfite plus 2.0 ml. working standard.

Add 5 ml. biuret reagent to all tubes. Let

*Available from Armour Pharmaceutical Company, Kankakee, Illinois, as Protein Standard Solution in 3 ml. sealed vials; prepared from crystallized bovine albumin.

(Continued on page A-30)


a single test
accurately detects
occult blood
in 1 minute
HEMOCCULT™
completes
the diagnostic
regimen...
In less than one minute HEMOCCULT detects the presence of occult blood. Used in testing both feces and urine, HEMOCCULT is sensitive enough to detect occult blood at trace amounts of 1:20,000. A compact and convenient test, HEMOCCULT can be used at bedside, as well as in the laboratory. Entire test procedure requires an inch of test paper, a drop of urine or a smear of feces and one or two drops of developer. In 30 seconds, you can read the results. A blue ring means a positive reaction; the thickness of the ring indicates the amount of occult blood present.
Supplied: HEMOCCULT test kit contains a roll of guaiac-impregnated test paper for 100 tests in plastic dispenser, one 10 ml. plastic bottle of developer and directions for use. All in compact carrying case.
Literature available on request.
Schieffelin & Co. / Since 1794
Pharmaceutical Laboratories Division, New York 3, N. Y.

stand 30 minutes before determining optical density at 550 mμ.

Lack of care in the use of ether in facilitating precipitation of globulins may lead, through denaturization of albumin, to falsely low values for albumin and A/G ratio. Saifer and Zymaris[11] found that use of Span-ether, gentle inversion, and keeping the free air space within 1 ml. avoided this hazard.

Comment

In conclusion, the fractionation of albumin and globulin depends in a critical fashion on the salt concentration to which serum is exposed in chemical fractionation methods. By electrophoresis, albumin and the globulins can be clearly separated. There are, however, many clinical applications for convenient methods of separation which are less time-consuming and laborious than the electrophoretic methods. Two rapid methods, the results of which agree well with values obtained by electrophoresis, have been mentioned; one has been described in detail.

It is important to keep in mind that the time-honored Howe method of fractionation gives albumin values which are too high and a falsely high A/G ratio. Many of the values in the literature for albumin and A/G ratio are based on determinations made by the Howe method. Some authors now specify this circumstance by referring to "albumin concentration (Howe)" and by making similar notations. Howe albumin has been found to contain some alpha-globulin. It would seem advisable for clinical laboratories generally to use a chemical method of fractionation which is in agreement with data obtained by electrophoretic separations. Change to a method of this type, of course, will affect the A/G ratio, and diagnostic interpretations based on this ratio will have to take this into account.

REFERENCES

1. Howe, P. E.: The determinations of proteins in blood. J. Biol. Chem. 49:109, 1921.
2. Tiselius, A.: Electrophoresis of serum globulin. II. Electrophoretic analysis of normal and immune sera. Biochem. J. 31:1464, 1937.
3. Majoor, C. L. H.: The possibility of detecting individual proteins in blood serum by differentiation of solubility curves in concentrated sodium sulfate solutions. Yale J. Biol. & Med. 18:419, 1946.
4. ——: The possibility of detecting individual proteins in blood serum by differentiation of solubility curves in concentrated sodium sulfate solutions; comparison of solubility curves with results of electrophoresis experiments. J. Biol. Chem. 169:583, 1947.
5. Milne, J.: Serum protein fractionation: A comparison of sodium sulfate precipitation and electrophoresis. *Ibid.*,[4] p. 595.
6. Reinhold, J. G.: Total protein, albumin and globulin. In Reiner, M. (Editor): Standard Methods of Clinical Chemistry. New York, Academic Press, Inc., 1953, vol. 1, p. 88.
7. Wolfson, W. Q., Cohn, C., Calvary, E. and Ichiba, F.: Studies in serum protein; a rapid procedure for the estimation of total protein, true albumin, total globulin, alpha globulin, beta globulin and gamma globulin in 1.0 ml. of serum. Am. J. Clin. Path. 18:723, 1948.
8. Kingsley, G. R.: A rapid method for separation of serum albumin and globulin. J. Biol. Chem. 133: 731, 1940.
9. Freier, E. F.: Fractionation of serum proteins. Chemistry laboratory procedures, University of Minnesota Hospitals. Unpublished data, September 1960.
10. Weichselbaum, T. C.: Determinations of proteins in blood serum and plasma. Am. J. Clin. Path. 16: 40, 1946.
11. Saifer, A. and Zymaris, M. C.: Effect of shaking on accuracy of salt fractionation methods for serum albumin. Clin. Chem. 1:180, 1955.

If you *Change* YOUR ADDRESS

Won't you please notify us as far in advance as possible. Send your old address together with the new.

Copies mailed to your old address will not be forwarded by the Post Office unless you provide the Post Office with the forwarding fee.

Send your change of address to

POSTGRADUATE MEDICINE
Essex Bldg., Minneapolis 3, Minn.

What's happening in Medicine

POSTGRADUATE MEDICINE'S REPORT of late news of interest to practicing physicians

TEACHING WITH PAYING PATIENTS

Association of American Medical Colleges:

• As the trend toward more universal medical insurance decreases the number of charity patients, the private paying patient will play an increasing role in the education of medical students, interns and residents. Over the last 33 years, private patients at the University of Chicago Clinics have enjoyed their contacts with the medical students. They recognize that an active teaching program results in better medical care. Only rarely does a patient complain about the number of times he must be examined. This is usually resolved by the tact of the resident staff.—Drs. Robert G. Page and Wright Adams, University of Chicago School of Medicine, Chicago.

• Data obtained from an intensive study of chronically ill patients in general hospitals, chronic disease hospitals, nursing homes, and homes for aged persons indicated that physicians have been slow to accept the contributions of other disciplines in providing comprehensive health care services. The need to develop new levels of care is apparent. These include rehabilitation, organized home-care programs, and improved intermediate-care institutions.—Dr. Francis E. Browning, University of Rochester School of Medicine and Dentistry, Rochester, N.Y.

SURGERY IN HEAD INJURY

Omaha Mid-West Clinical Society:

• The usual indications for surgery in head injuries, compound depressed fractures of the skull and extradural and subdural hematomas, are readily recognized. However, many head injuries present atypical pictures resulting in indecision regarding surgery. Useless surgery obviously should be avoided. The problem has been resolved by carotid arteriography, which quickly and safely localizes extradural, subdural and intracerebral hematomas. the surgical evacuation of which is lifesaving.—Dr. William P. Williamson, University of Kansas School of Medicine, Lawrence-Kansas City.

• The assumption that dyspareunia is primarily a manifestation of an emotional problem proved to be fallacious in a study of a large number of women complaining of painful coitus. Actually dyspareunia is a relatively common symptom of congenital anomalies of the genitalia and of several different organic lesions. Sometimes it is a functional disorder, but, if properly interpreted, it may also be a significant diagnostic signal of a major pelvic disorder.—Dr. John W. Huffman, Northwestern University Medical School, Chicago.

Regeneration of neural tissue

United Cerebral Palsy Association:

- Sterilization of homografts by radiation enlarges the possibilities of storing frozen nerves in banks comparable to the existing bone and blood vessel banks. It is planned to bank nerves acquired from autopsies of patients with no recent history of cancer or serious viral disease. These homografts will be frozen and then sterilized. In several hundred experiments, homografts of peripheral nerves were introduced into gaps in the feline peripheral nerve, the nerve ends and intervening space being encased in a sheath of Millipore. There was no evidence of a homograft reaction, and satisfactory muscular function was ultimately restored.—Dr. James B. Campbell, Columbia University College of Physicians and Surgeons, New York.

Interferon versus viruses

National Academy of Sciences:

- Protein interferon, produced by cells exposed to virus particles, permits the cells to resist infection indefinitely. Interferon competes with the virus for susceptible cells. If the virus gains in concentration, more interferon is produced, thus reducing further spread of the infection. Protection by interferon is transitory, however, and when its effect wears off, the virus can again be replicated. Interferon and virus keep each other in balance, so that both virus and cells survive simultaneously and indefinitely in culture. Efforts are being made to isolate and characterize interferon from various sources and to study the spectrum of its activity against various viruses in the expectation that it may prove valuable in controlling some viral infections.—Dr. Werner Henle, University of Pennsylvania School of Medicine, Philadelphia.

- An abnormal chromosome has been found in the cells of one type of human leukemia. In all seven cases of chronic granulocytic leukemia thus far investigated, one of the chromosomes in the leukemic cells has been found to be unusually small. Apparently a portion has been lost from this chromosome. This change may be the cause of the malignant nature of these cells. In two other types of human leukemia, acute granulocytic and acute childhood leukemia, no chromosome change has been found. If the fundamental abnormality in these diseases is in the chromosomes or their parts, the change apparently is too small to be seen without more refined methods.—Drs. Peter C. Nowell and David A. Hungerford, University of Pennsylvania School of Medicine and Institute for Cancer Research, Philadelphia.

Treatment of gastric ulcer

Radiological Society of North America, Inc.:

- The opinion that all gastric ulcers should be treated by some form of gastric resection is widely held. This is based primarily on doubt in the ability to differentiate the benign from the malignant ulcer and on the belief that the operative mortality and postoperative morbidity are outweighed by the number of cured patients. Radiologic and gastroscopic examination provides reliable evidence concerning the type of ulceration. Since it is debatable that a patient with benign disease will be better off with all or part of his stomach removed, a clinical evaluation should be used to determine the candidate who may respond to medical therapy.—Dr. Gerald D. Dodd, Jr., Houston.

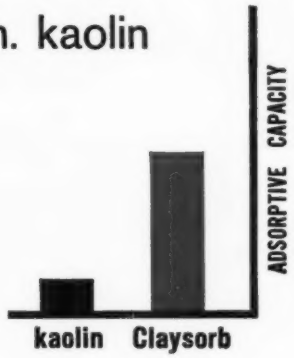
- In treating intrathoracic neoplasms and postoperative breast carcinomas, particularly with supervoltage radiation therapy, doses of more than 3500 r may be administered in the cardiac area. Although cardiac damage may be induced, it appears of such insignificance that modification of adequate present-day radiotherapeutic technics is not justified.—Dr. Jerome M. Vaeth, San Francisco.

POLYMAGMA

claysorb, superior adsorbent, plus 2 antibiotics

Claysorb adsorptive capacity is 5x greater than kaolin[1]

2 gm. Claysorb = 10 gm. kaolin



- POLYMAGMA stops diarrhea promptly, conveniently, comfortably
- helps restore normal intestinal function
- promotes physiologic stools
- soothes irritated intestinal mucosa
- 98-99% of human enteric viruses were adsorbed by CLAYSORB in recent *in vitro* study[2]

POLYMAGMA

provides bactericidal action against pathogens

- polymyxin and dihydrostreptomycin provide synergistic bactericidal action against most enteric pathogens
- POLYMAGMA destroys pathogens, controls diarrhea, and makes patients comfortable

to control uncomplicated diarrhea

DIAMAGMA®

CLAYSORB® (Activated Attapulgite, Wyeth) and Pectin in Alumina Gel, Wyeth (formerly POLYMAGMA® Plain)

contains claysorb for superior adsorbent action

1. Barr, M., and Arnista, E.S.: J. Am. Pharm. A. (Scient. Ed.) *46*:493 (Aug.) 1957. 2. Bartell, P., Pierzchala, W., and Tint, H.: J. Am. Pharm. A. (Scient. Ed.) *49*:1 (Jan.) 1960.

For further information on limitations, administration, and prescribing of POLYMAGMA or DIAMAGMA, see descriptive literature or current Direction Circular.

Wyeth Laboratories — Philadelphia 1, Pa.

Wyeth® SERVICE TO MEDICINE

Forensic Medicine

The Cardiac: Industry's Medicolegal Problem

OLIVER C. SCHROEDER, JR.*

Editorial Comment

The most important single legal event uniting law and medicine in the administration of justice has been the enactment of workmen's compensation laws. Many doctors have not participated in justice procedures as expert medical witnesses, the physician's historic role. Few doctors, however, have not examined compensation patients and filed reports for compensation awards. This article emphasizes a most difficult problem confronting the physician with a cardiac patient who needs to earn his livelihood not only for economic but also for therapeutic reasons. The employer facing legal obligations may not accept the cardiac worker. To illuminate this area is the intent of the following article.

THE past half-century within our nation has witnessed the birth and growth of social legislation. Traditional common-law rules, used for centuries, were eliminated in particular areas of human activity. The employment relationship introduced the first such statutes—workmen's compensation. Employees injured or diseased as the result of employment were to receive medical care and compensation payments; if killed, the dependents were to receive payments. In addition to legal interests, these statutes involved economic, social and medical interests as well: economic because the costs were borne by industry in an insurance program as a cost of production; social because the injured or diseased worker was to be restored to his social position as a producer in society; medical because all injured or diseased employees were to have available diagnostic, therapeutic and rehabilitative procedures. Medicine and law were truly cast together by this legislation. Furthermore this casting also involved economic and social matters of prime importance.

In the past five decades of industrial growth and medical progress, the implications of workmen's compensation have changed. Modern industrial technology demands healthy employees. Many employees, through aging processes and accelerated living conditions, have America's number one ailment—heart disease. The laws involving heart disease in workmen's compensation cases are not difficult to state:[1]

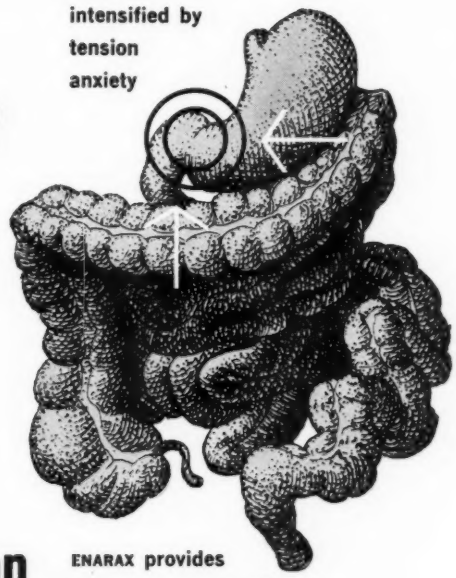
1. Disability due to a heart condition is compensable when that disability arose out of

(Continued on page A-42)

*Director, The Law-Medicine Center, and Professor, School of Law, Western Reserve University, Cleveland, Ohio.

double trouble of the g.i. tract?

spasm
hyperacidity
pain...
intensified by
tension
anxiety



dual action in the therapeutic attack

ENARAX provides
10 mg. oxyphencyclimine
the inherently
long-acting anticholinergic
plus 25 mg. ATARAX®†
the tranquilizer
that does not stimulate
gastric secretion

ENARAX®

A SENTRY FOR THE G.I. TRACT **B.I.D.**

Proven effective for continuous relief of both physical and emotional aspects of G.I. disease — hypermotility, hyperacidity, and hyperemotivity. One tablet b.i.d. provides 24-hour control of symptoms in peptic ulcer, gastritis, gastroenteritis, colitis, functional bowel syndrome, duodenitis, hiatus hernia (symptomatic), irritable bowel syndrome, pylorospasm, cardiospasm, biliary tract dysfunctions, and dysmenorrhea. ENARAX has been successful in 92% of cases.[1-3] Let your G.I. patients profit from its dual, full-time therapeutic action.

Dosage: One-half to one tablet twice daily — preferably in the morning and before retiring. The maintenance dose should be adjusted according to the therapeutic response. Use with caution in patients with prostatic hypertrophy and only with ophthalmological supervision in glaucoma. **Supplied:** In bottles of 60 black-and-white scored tablets. Prescription only.

References: 1. Hock, C. W.: Am. J. Gastroenterol. 34:293 (Sept.) 1960. 2. Leming, B. H., Jr.: Clin. Med. 6:423 (Mar.) 1959. 3. Data in Roerig Medical Department files.

†brand of hydroxyzine

FOR HEMATOPOIETIC STIMULATION WHERE OCCULT BLEEDING IS PRESENT **HEPTUNA®** PLUS THE **COMPLETE** ANEMIA THERAPY

ROERIG

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being™

and in the course of employment as the result of an accident.

a. A few jurisdictions require the disability to be *caused* by an accident—a sudden, unexpected, unusual, external force: a girder falling across the worker's chest and compressing the heart.
b. Most jurisdictions recognize disability when the *result* is sudden, unusual and unexpected: a heavy lifting which severely strains the heart.
   (1) When overexertion activates or aggravates a pre-existing heart condition into a disability most states provide compensation benefits.
   (2) When the exertion is normal for an average worker but overexertion for a worker with a diseased heart, courts are divided on the issue of whether or not to provide benefits.
   (3) In some states where an employee has a chronic heart condition which has developed to the place where death could result from any exertion, if the employee dies while doing ordinary work, no compensation benefits are allowed.

These legal rules reflect the major challenges to law and medicine in the cardiac worker's problem. What causes the heart disability—the employment experience or life's aging process? How do you identify, measure and evaluate the heart disability? Can law and medicine cooperate to aid industry in better handling of the cardiac worker? What are the experiences and attitudes of industry regarding the cardiac worker?

We shall direct our attention to this last question. To know where we are is the prerequisite for determining where we should go. Over the past decade and a half numerous studies of this dynamic problem have been conducted. All contribute vital data to answer the question to be considered.

In Massachusetts from 1948 to 1952 workmen's compensation experience revealed an increase of cardiac cases as a percentage of all permanent and total disability cases from 3.2 to 5 per cent. While such claims were not of major concern, claims for death benefits were. In the same period the cardiac death claims increased from 24 per cent of all death claims to 37 per cent. The benefits paid increased from $251,646 to $688,953. One conclusion of the study of cardiac worker employment in the Greater Boston area was that "the threat and potential risk of workmen's compensation costs appear to be the primary deterrent to employment of persons with heart diseases."[2]

Experiences in other jurisdictions also underscore this vexing problem.

Two extensive surveys on the impact of the cardiac in industry are available for comparison. In Minnesota a survey by Mathy[3] and in Ohio one by this author merit close comparison. Both were conducted in 1958 and 1959.

	MINNESOTA	OHIO
Questionnaires sent	235	172
Questionnaires returned	118	52
Percentage of returns	50%	30%

In Ohio 10 other employers replied with such meager data that their questionnaires were excluded.

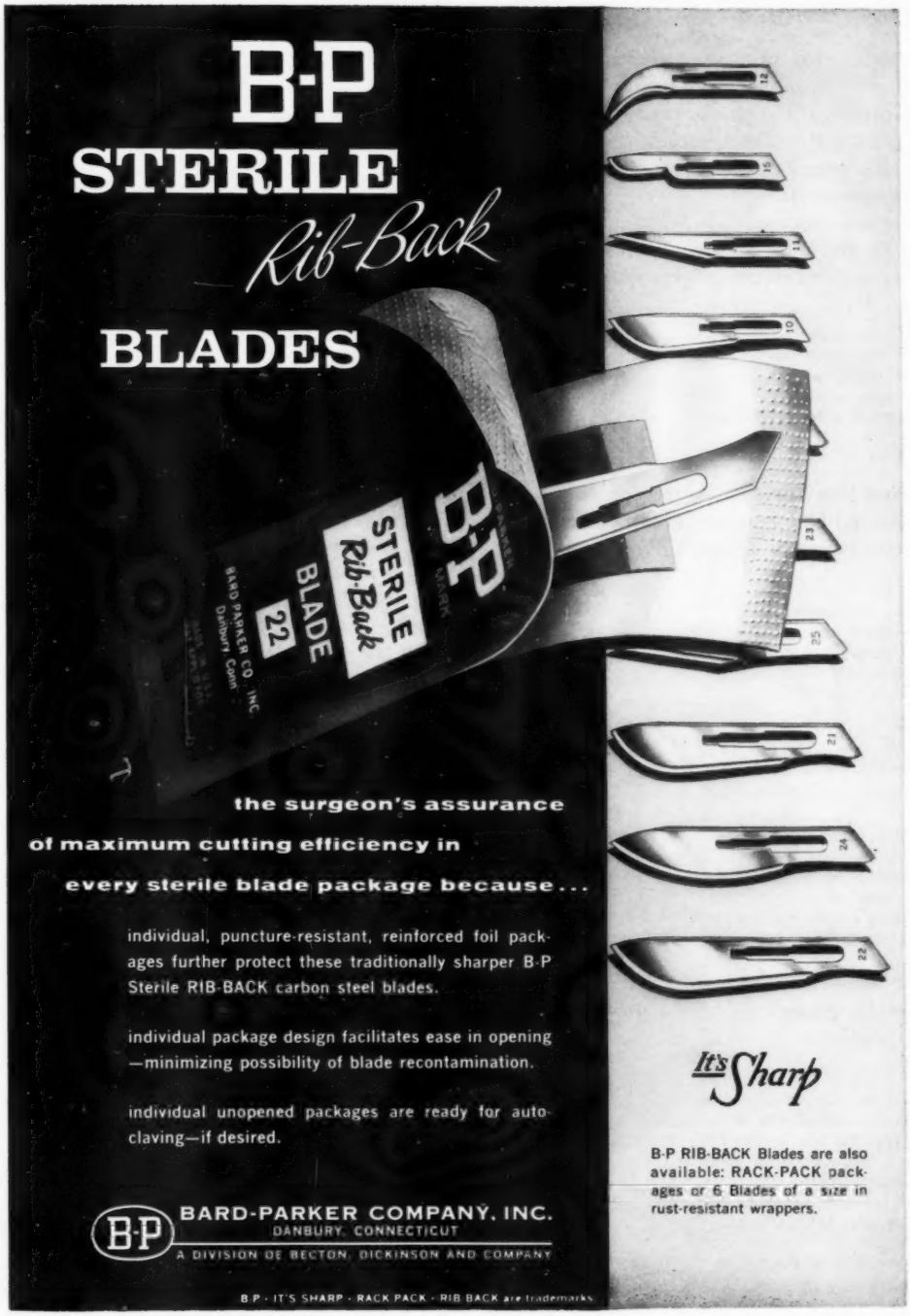
The Minnesota survey was conducted by the Minnesota Department of Health in conjunction with the state medical association with emphasis on the medical problem of rehabilitation. The Ohio survey was conducted by me through workmen's compensation representatives of self-insuring employers. Undoubtedly the latter group was more sensitive to compensation costs and claims dangers, so publicity was not welcomed; hence a lower return of the questionnaires in Ohio is understandable. The Ohio returns represented more complete answers than the Mathy survey produced, however. When an employer replied, each question was answered.

The number of employees with heart disease known to the employers is surprisingly similar.

	MINNESOTA	OHIO
Total employees of employers replying	76,805	116,587
Known cardiacs	1,708	2,266
Percentage of employees with known heart disease	2.2%	1.9%

(Continued on page A-44)

B-P STERILE *Rib-Back* BLADES



the surgeon's assurance of maximum cutting efficiency in every sterile blade package because...

individual, puncture-resistant, reinforced foil packages further protect these traditionally sharper B-P Sterile RIB-BACK carbon steel blades.

individual package design facilitates ease in opening —minimizing possibility of blade recontamination.

individual unopened packages are ready for autoclaving—if desired.

It's Sharp

B-P RIB-BACK Blades are also available: RACK-PACK packages of 6 Blades of a size in rust-resistant wrappers.

B-P BARD-PARKER COMPANY, INC.
DANBURY, CONNECTICUT
A DIVISION OF BECTON, DICKINSON AND COMPANY

B-P · IT'S SHARP · RACK-PACK · RIB-BACK are trademarks

The actual prevalence of heart disease among employees would undoubtedly be much higher, however. The average percentage of cardiacs in the total population is 10 per cent in the adult population. Undoubtedly many employees with heart disease have never been so identified by their employers even in self-insuring companies which are most sensitive to compensation costs.

Figures representing heart attacks occurring on and off the job indicate substantially the same percentages in both states.

	MINNESOTA	OHIO
Total employees represented	75,530	116,587
Heart attacks on job	81	89
Heart attacks off job	311	455
Total heart attacks	392	544
Percentage of heart attacks		
On job	21%	19%
Off job	79%	81%

Fatal heart attacks on the job in the Minnesota and Ohio studies reveal a considerable difference in percentage.

	MINNESOTA	OHIO
Employees represented	75,530	116,587
Total heart attacks on job	81	89
Fatal cases	18	28
Percentage of fatal cases to on-job heart attacks	22%	31%

The figures on workmen's compensation claims arising from on-the-job heart attacks represent a similar variance.

	MINNESOTA	OHIO
On-the-job heart attacks	81	89
Workmen's compensation claims filed	10	7
Percentage of claims arising	12%	8%
Workmen's compensation claims awarded	5	2
Percentage of awards to claims filed	50%	29%

Cardiacs who return to work after heart attacks represent a substantial majority in both studies.

	MINNESOTA	OHIO
Total heart attacks on and off the job minus fatalities (Minnesota survey did not specifically request this figure but many employers supplied it)	365	535
Employees who returned to work after heart attacks	239	388
Percentage of employees who returned to work	66%	73%

Lost time to business and industry in one year on the basis of weeks lost appears to be about the same span.

	MINNESOTA	OHIO
Total employees	67,114	116,587
Employees with known heart disease	1,595	2,266
Weeks lost	4,073	5,446
Average time lost for each known cardiac in weeks	2.5	2.4

Policies regarding the return to work of employees after recovering from a heart attack reveal similar attitudes by employers in both states. Nearly 50 per cent of the Minnesota employers return the worker to his former job or selectively place him in a job commensurate with his physical ability. In Ohio these policies are accepted by 75 per cent of the self-insuring employers. No Ohio employer admitted to a policy of requiring the employee to seek work elsewhere, but 23 per cent stated that the employee was given a suitable job *if available*. In Minnesota 2.6 per cent of the employers have a policy of requiring the employee to seek work elsewhere and 16 per cent admit to a policy of giving a suitable job *if available*.

When it comes to a hiring policy, however, cardiac workers in both states are met with much severer policies.

	MINNESOTA	OHIO
Never hire	32%	29%
Seldom hire	27%	35%
Occasionally hire	18%	23%
Regularly hire	3%	4%

Reluctance toward the hiring of cardiacs stems from several sources.[4] Foremost is the belief that the physical demands of the job are greater than the physical ability of the worker with heart disease. A close second is the lack of a suitable job. Both Minnesota and Ohio present this picture. In Ohio 60 per cent of the employers place these two reasons first or second. In third and fourth position employers in both states revealed the concern over workmen's compensation liability and company-sponsored sickness and accident insurance or sick leave liability. In Ohio 24 per cent of the employers rated these reasons first and second. In Minnesota, when queried why they ranked the policy reasons for hiring car-

(Continued on page A-46)

ACTH

basic in medicine

Cortrophin®-Zinc

(corticotropin-alpha zinc hydroxide, Organon)

best in practice

free-flowing / convenient / non-irritant / quickly absorbed / uniform release / even activity / 2-3 day effect / minimal risk

CORTROPHIN-ZINC is preferred in severe bursitis, resistant asthma, and other ACTH indications because physicians know it as the most refined, longest-acting corticotropin . . . of unequalled purity, safe, reliable, and consistently uniform in action. Easily and quickly given with a small-bore needle, this free-flowing aqueous suspension exerts full therapeutic influence quickly, maintains it evenly for 2 to 3 days.

Supplied: 40 U.S.P. units/cc., 5-cc. vials, 1-cc. sterile, disposable syringes; 20 U.S.P. units/cc., 5-cc. vials.

Organon **Organon Inc.,** West Orange, N. J.

diacs in the order presented, smaller employers placed lack of a suitable job first and fear of workmen's compensation and group insurance claims second. Larger employers consistently ranked the second reason first. In Ohio the primary reasons were submitted by employers as follows:

Physical demand of job greater than employee's physical ability	31%
Lack of suitable job	30%
Company sickness and accident insurance	16%
Workmen's compensation liability	6%
Other	4%

Where Ohio employers took the liberty of writing brief comments they overwhelmingly emphasized the physical demands of the job and the fear of increased financial costs from compensation claims and insurance payments.

Actual costs to employers present interesting comparisons.

	MINNESOTA	OHIO
Workmen's compensation claims in 1957 arising out of cardiac claims	$ 4,515.00	$ 11,038.00
Group insurance and sick leave payments	$544,988.54	$882,448.76

Workmen's compensation payments in Ohio represent slightly more than 1.2 per cent of the total amount paid by employers for cardiac claims, while in Minnesota the payments represent less than 1 per cent, pending claims excluded. The almost negligible amount of workmen's compensation payments does not reflect the truth of the attitude of fear expressed by employers over workmen's compensation liability.

Perhaps another Ohio study of death claims involving cardiac workers in workmen's compensation will emphasize the reason for this apparently excessive fear which generates the "no hiring" policy.

In 1956, 189 workmen's compensation death claims involving cardiacs were filed (184 males, 5 females); in 1957, 219 such claims (216 males, 3 females); in 1958, 136 such claims (135 males, 1 female). A negligible number—less than 2 per cent—were apparently awarded death benefits directly because of the cardiac condition. This figure is deceptive, however, because the heart disease unknowingly may have set the stage or even precipitated the experience which resulted in an industrial injury followed by death. Employers' fears of higher costs rest on this unknown factor.[5] In addition, the determination of a death award or even a cardiac injury and illness by a public body subject to social and economic pressures rather than a medical body subject to scientific facts contributes to the unknown outcome and emphasizes the employers' fears in hiring cardiac workers.[6]

Other studies have contributed additional facts and conclusions to the problems of legal liabilities, financial costs and the cardiac workers.

In the surveys by Kline[7] in 1954 for the United States, Olshansky et al.[2] in 1955 for the Greater Boston area, and by Lee et al.[8] in 1957 for the United States, facts and conclusions surprisingly similar to the later Minnesota and Ohio studies were revealed. These were as follows:

1. The precise number of cardiac employees is not known and the number reported is probably a gross understatement. Lee and his associates reported the highest number, 8 per cent.

2. Heart attacks among cardiac workers occur overwhelmingly, 75 to 87 per cent, in off-the-job periods.

3. Cardiac employees who have had an attack return to their employers in the majority of cases, 66 to 80 per cent.

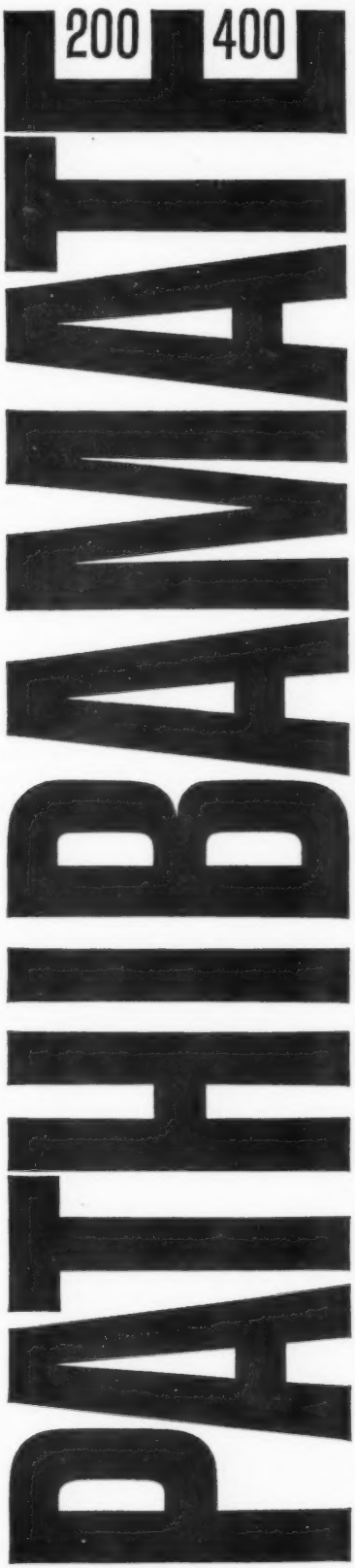
4. Few cardiac workers are hired by employers: 99 cardiacs out of 13,431 hirings studied by Olshansky et al.; 242 out of 19,321 hirings studied by Lee et al.

5. Employers have adopted stated policies of accepting their own employees back after a heart attack but refusing to hire new cardiac workers.

6. Workmen's compensation liability, sickness and health insurance liability, and lack of a suitable job are the primary expressed reasons for the "no hiring" of cardiac workers.

7. Fears of potential costs of workmen's compensation and of sickness and health insurance are increasing in importance to em-

(Continued on page A-48)



for
real or potential
ulcer...

PATHIBAMATE®

meprobamate with PATHILON® tridihexethyl chloride Lederle

anticholinergic . . .
treats the trauma
tranquilizer . . .
controls the tension

Indications: duodenal ulcer; gastric ulcer; intestinal colic; spastic and irritable colon; ileitis; esophageal spasm; anxiety neurosis with gastrointestinal symptoms, and gastric hypermotility.

Administration and Dosage: PATHIBAMATE-400 (full meprobamate effect)—1 tablet three times a day at mealtime, and 2 tablets at bedtime. PATHIBAMATE-200 (limited meprobamate effect)—1 or 2 tablets three times a day at mealtime, and 2 tablets at bedtime. Adjust to patient response.

Contraindications: glaucoma; pyloric obstruction, and obstruction of the urinary bladder neck.

Lederle

LEDERLE LABORATORIES
A Division of AMERICAN CYANAMID COMPANY
Pearl River, New York

ployers in their policy toward hiring cardiacs.

8. Actual workmen's compensation costs are minimal but are increasing; sickness and health insurance costs are many times more expensive than workmen's compensation and are also increasing. It should be acknowledged, however, that at least one authority does not consider workmen's compensation costs for cardiac claims to be incidental and unimportant.[9] In 1949, heart compensation cases in New York state represented only 0.18 per cent of the total compensation cases but the costs represented 2.5 per cent or one-fortieth of all compensation costs.

One general conclusion deserves special emphasis. Legal implications involving employers' costs are affecting the cardiac in business and industry and these implications are growing in importance. The most graphic example of this concern over rising costs can be found in the state of New York. A governor's commissioner has recently completed two reports on the costs, operations and procedures of the New York workmen's compensation law.[10] One crucial area studied was that of cardiac cases where a steady rise in the number and a steady increase in the cost have caused much concern and criticism.

In trying to determine medical facts and opinions the commissioner surveyed 398 doctors from a nationwide group of medical specialists of whom 206 (51.8 per cent) had a subspecialty in cardiovascular diseases. These interesting conclusions were obtained by the indicated percentages:[11]

1. Work does not produce heart disease (93.9% against 1.5%).

2. Coronary arteriosclerosis or some other form of coronary disease must have pre-existed in an individual who suffers a coronary occlusion and myocardial infarction (93.4% against 6.3%).

3. Performance of the same type of moderately heavy work without engaging in unusual exertion or strain has no injurious effect upon the heart. A myocardial infarction occurring during such work is not causally related to the employment (88.6% against 7.1%).

4. Subsequent attacks of myocardial infarction are not causally related to the first attack, but to the underlying pathology of the coronary vessels in the heart (82.9% against 12.9%).

5. Opinion on the effect of strenuous physical exertion or emotional disturbance upon the heart was divided; 46.6% considered that there was a causal relationship between strenuous work and an ensuing myocardial infarction; 49.5% did not. The general opinion was that the emotional factor plays a more important role in bringing on such an attack than the physical.

6. Opinion was divided on whether a person has a permanent partial disability after he has recovered from his myocardial infarction and returned to work and is asymptomatic; 45.8% felt that there was a disability and 47.9% that there was not.

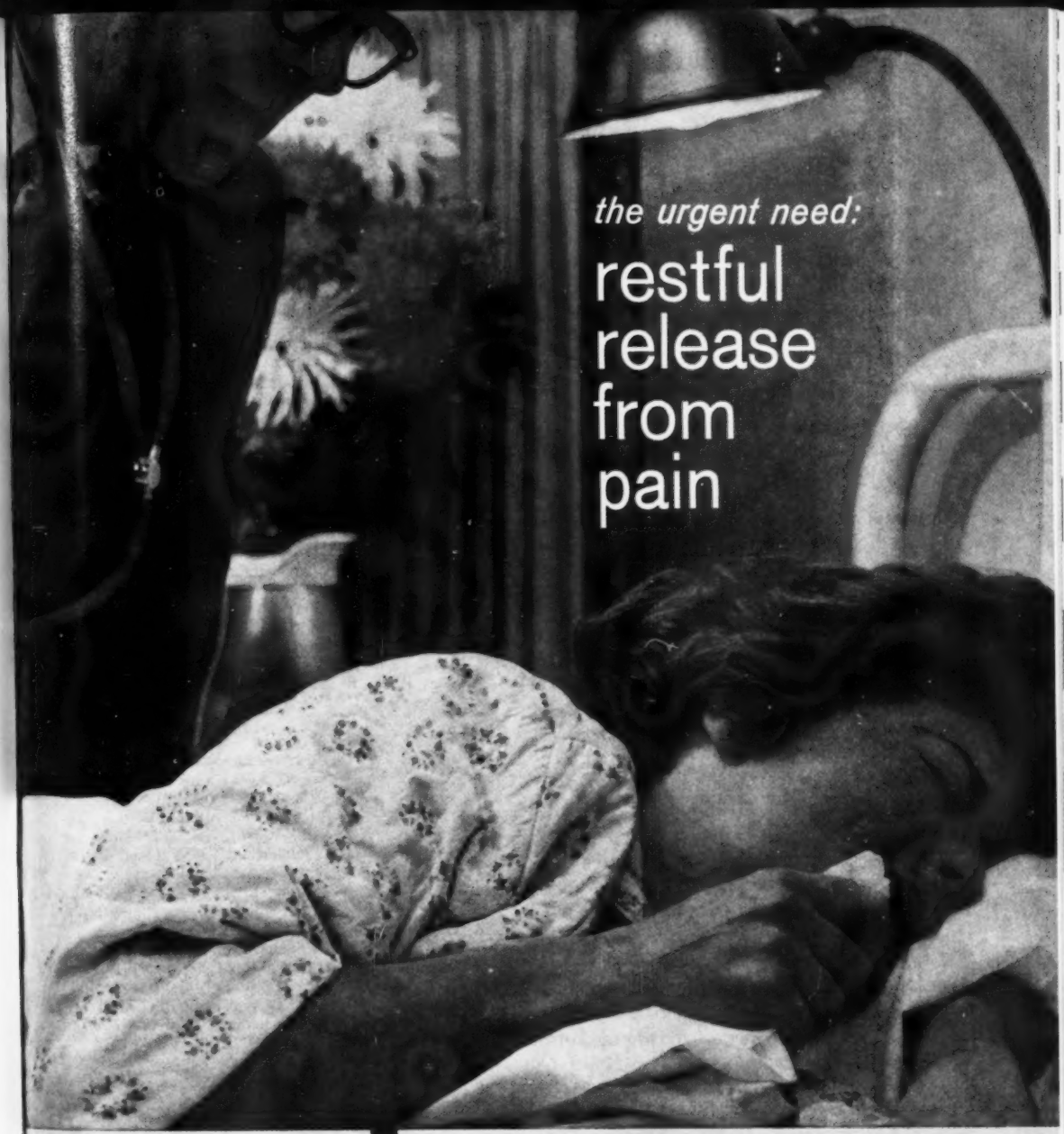
The important conclusions in numbers 5 and 6 just quoted reflect the two most important legal issues in workmen's compensation practice—the causal relationship between stress and strain and the extent of disability. Medical scientists themselves are surprisingly evenly divided. No wonder that lay boards, commissions and hearing officers in workmen's compensation work have difficulty in providing a "correct" legal decision.

In concluding his second report the commissioner also emphasized the importance of the cost factor in workmen's compensation:[12]

> New York is, thus, shown to be the highest cost state for self-insurers as well as for carriers. Permissible benefits are no higher and, of course, accident frequency and severity no greater for self-insurers than for others. The higher cost in New York is not producing greater benefits for deserving disabled workers but is being consumed at least in part by high administrative and/or medical costs and the payment of claims that would not pass elsewhere.

Workmen's compensation experience reveals that direct benefits paid to workers injured or killed as the result of their work are not the whole cost to business and industry. For every dollar paid in benefits arising out of an employment injury or death, another

(Continued on page A-50)



AHR **PHENAPHEN**
(Basic formula)

In each capsule: Phenacetin (3 gr.) 194.0 mg.; acetylsalicylic acid (2½ gr.) 162.0 mg.; hyoscyamine sulfate 0.031 mg.; and phenobarbital (¼ gr.) 16.2 mg.

AHR **PHENAPHEN No. 2**
PHENAPHEN with Codeine ..... ¼ gr.

AHR AHR **PHENAPHEN No. 3**
PHENAPHEN with Codeine ..... ½ gr.

AHR **PHENAPHEN No. 4**
PHENAPHEN with Codeine ..... 1 gr.

SUPPLY: Bottles of 100 and 500 capsules.

sedative-enhanced analgesia

To each "according to his need" — maximum safe analgesia through time-and-pain-tested synergistic formulations, in four strengths for individualized prescription.

PHENAPHEN® Robins

PHENAPHEN® WITH CODEINE

¼ gr., ½ gr., 1 gr.

A. H. ROBINS CO., INC., Richmond 20, Virginia

Making today's medicines with integrity . . . seeking tomorrow's with persistence

three dollars represent the indirect cost to the employer in loss of production time, damage to machinery or equipment, training new personnel, and similar expenses.[13] These hidden costs also become deterring factors to employment of persons with cardiac complaints.

On the other hand, a well-developed rehabilitation program is credited with measurable reductions in compensation costs to employers. Dr. E. C. Steele[14] of the Ontario Workmen's Compensation Board has stated:

> We feel, although we have no way of proving it, that the six or seven million dollars spent in building, landscaping and equipping our (Rehabilitation) Centre will be returned twentyfold in savings of compensation costs to the employers in this Province. For those of you who are interested, or dubious, I would refer you to the medical report presented to this association in 1953. At that time Ontario had the lowest ratio of permanent disability awards to the total number of compensation cases in the United States or Canada. The exact figure was 3.77%. That is, of all claimants having industrial accidents only 3.77% received permanent disability awards. We attribute this to our rehabilitation programme which includes, as mentioned previously, expert medical care.

In a free economic society, concern over costs of production is paramount. Costs measure efficiency, efficiency produces profits, profits nurture the economy. The cardiac worker represents a hidden medical danger to industrial costs. To cast light on the truthful facts relating to these workers is a primary duty of law and medicine. The expansion of medical knowledge in the area of heart disease is needed, especially as it pertains to the family doctor and general practitioner. Beneath this expansion is the medical research now so active in the cardiac area. Once these matters are in hand, the therapy and rehabilitation of the cardiac worker will be forthcoming. To the cardiac employee, rehabilitation means not only medical care but also social and economic adjustment. All three factors are interdependent. The law, simultaneously, must create the legal atmosphere conducive to stimulating these rehabilitative forces. In a nation whose foremost public health problem is heart disease, these challenges to law and medicine represent dynamic opportunities to unite in serving our society.

REFERENCES

1. Schneider, W. R.: Workmen's Compensation Text. St. Louis, Thomas Law Book Co., 1946, vol. 5, pp. 116-154; cumulative supp. 3, 1959, pp. 28-35.
2. Olshansky, S., Friedland, S., Clark, R. J. and Sprague, H. B.: A survey of employment policies as related to cardiac patients in Greater Boston. New England J. Med. 253:506, 1955.
3. Mathy, W. E.: Survey of cardiovascular disease in industry in the state of Minnesota. Minnesota Med. 41:805-811 (November) 1958.
4. Employment and Heart Disease. Proceedings of First Western Conference, California Heart Association, March 18-19, 1955.
5. Pinto, S. H.: Heart disease and workmen's compensation. A.M.A. Arch. Indust. H. 17:437, 1958.
6. Keiper, J. S.: Forces That Spiral Workmen's Compensation Costs. New York, Commerce and Industrial Association of New York, Inc., 1953.
7. Kline, E. M.: Heart disease and employment. Indust. Med. 23:126 (March) 1954.
8. Lee, P. R., Rusk, H. A., White, P. D. and Williams, B.: Cardiac rehabilitation. J.A.M.A. 165: 787, 1957.
9. Keuhof, A. C.: Problems of the Employment of the Cardiac in Industry. New York, American Heart Association, 1957.
10. Callahan, J. M.: Costs, Operations and Procedures Under the Workmen's Compensation Law of the State of New York. Report No. 1 to Governor Averell Harriman, January 28, 1957; Report No. 2, December 29, 1958.
11. *Ibid.*,[10] Report No. 1, pp. 104-120.
12. *Ibid.*,[10] Report No. 2, p. 86.
13. Oral testimony presented by private insurance carriers to the Ohio Program Commission, Committee to Investigate Workmen's Compensation, 1949-1950.
14. Panel discussion on rehabilitation given at the 10th convention, International Association Industrial Accidents Boards and Commissions, St. Paul, September 25, 1957.

MEETINGS and Postgraduate Courses

University of California Medical Center, San Francisco: Conferences to be held in March include:

Diseases of the nervous system in childhood, 2-3
Urology
Perinatal problems
Diagnostic radiology
Evening lectures for physical therapists
Evening lectures for pharmacists (Sacramento)
The dietitian—her orbit of influence (Asilomar)

For further information, write to: Continuing Education in Medicine, University of California Medical Center, San Francisco 22.

Radiology FOR PRACTICING PHYSICIANS

Intensification of the Fluoroscopic Screen

RUSSELL H. MORGAN

The Johns Hopkins University, Baltimore

RUSSELL H. MORGAN

Dr. Russell H. Morgan, professor of radiology, The Johns Hopkins University, and radiologist-in-chief, The Johns Hopkins Hospital, was born in London, Ontario, in 1911 and became a citizen of the United States in 1943. He received his B.A. and M.D. degrees from the University of Western Ontario, and in 1938 completed an internship at Harper Hospital, Detroit. From 1938 to 1940 he was a resident in pathology at St. Luke's Hospital, Chicago, and from 1940 to 1942, a resident in radiology at the University of Chicago.

*On completing his training in radiology, Dr. Morgan was first an instructor, then assistant professor and afterward associate professor of radiology at the University of Chicago. From 1944 to 1946, he was with the United States Public Health Service, with the rank of commander. He was appointed to his present posts in 1946.—Paul C. Hodges, M.D.**

*Emeritus Professor and Chairman, Department of Radiology, University of Chicago, Chicago, Illinois. POSTGRADUATE MEDICINE's Editor for this Section on Radiology.

THE recent development of methods[1-5] whereby the brightness of x-ray fluoroscopic screens may be increased from several hundred to several thousand times, without an increase in the x-ray dose rate to the patient, is likely to have a profound effect on the practice of medicine. With the increase in screen brightness have come substantial improvements in the clarity of fluoroscopic vision, the elimination of the need for dark adaptation, and, under some circumstances (particularly in fluoroscopy of children and of the adult chest), a reduction of the radiation dose rate delivered to patients.

In addition to its influence on fluoroscopy, screen intensification has made practical for the first time the recording of physiologic phenomena by cinefluorography. Until this new development, the radiation doses needed to obtain satisfactory cinefluorograms were so large that x-ray motion pictures were made of patients only under very limited circumstances.

In view of the impact of bright-screen fluoroscopy in medicine, it may be worthwhile to review the methods by which screen intensification has been achieved and the research which is currently in progress to develop new

and better instruments. Before doing so, however, let us study the factors which control the clarity of fluoroscopic vision. From such an examination will be gained a better understanding of the fluoroscopic process and thereby a better understanding of how screen-intensification instruments operate.

Clarity of Fluoroscopic Images

Over the years, a copious literature has accumulated which indicates that the clarity of fluoroscopic vision is controlled by the grain size of the fluoroscopic screen, the size of the focal spot of the x-ray tube, and a number of factors associated with the characteristics of the human eye.[3,6-8] Although all these factors impose limitations on the clarity with which fluoroscopic images are visualized, there is yet another factor which is even more fundamental.[9,10]

The image appearing on a fluoroscopic screen is produced by the projection of an x-ray beam, composed of myriads of x-ray photons or quanta, through the anatomic structure which one wishes to visualize. On passing through the structure, many and usually most of these photons are absorbed or scattered and hence are lost to the fluoroscopic process; however, some pass through the structure to emerge on the other side and then to fall on the fluoroscopic screen. On the screen, they are converted to light, and hence may be seen.

It will be clear from the foregoing that the diagnostic information contained in a fluoroscopic image is carried from the patient to the screen by the photons which comprise the x-ray beam. Indeed, each photon transmitted from patient to screen may be considered to carry a certain small amount of diagnostic information. Therefore, the larger the number of photons in the x-ray beam, the greater will be the diagnostic information available to the fluoroscopist. Now, a screen which yields a large amount of information inherently exhibits greater detail than does a screen with a low informational yield. Therefore, fluoroscopic clarity is a direct function of the number of x-ray photons taking part in the fluoroscopic process.

That this is true may be easily demonstrated if one fluoroscopes a patient first with an x-ray tube current of 0.5 ma and then with a current of 5 ma. Since the number of x-ray photons projected through the patient is directly proportional to the tube current, greater detail should be observed at the higher milliamperage. When the experiment is performed this is exactly what is observed. This demonstrates rather nicely perhaps that the grain size of the fluoroscopic screen and the focal spot of the x-ray tube are not fundamental controlling factors affecting fluoroscopic clarity or detail. If grain size, for example, were the controlling factor, the increase in milliamperage from 0.5 to 5 ma would not produce any change in the visible detail whatever.

When the current flowing through an x-ray tube is increased, the radiation dose rate increases proportionately. Since conventional fluoroscopic practice employs tube currents which yield dose rates considered to be at the upper limits for patient safety, improvements in the clarity of fluoroscopic images achieved by an upward revision of tube-current settings are not permissible.

The question may now be asked as to what happens to fluoroscopic clarity if one brightens the screen, not by increasing the milliamperage of the x-ray tube but by replacing the conventional screen with one of the new instruments which brighten the fluoroscopic process. On the basis of the preceding discussion, it might appear that no increase in clarity should occur. Even if the fluoroscopic screen is made brighter by an intensification device, the current flowing through the x-ray tube and hence the number of x-ray photons passing through the patient are not increased. Therefore, no more diagnostic information is carried from patient to screen and no improvement in screen clarity should occur. This reasoning, however, will only be valid if the eye in conventional fluoroscopy utilizes 100 per cent of the information available to it. If the eye is not 100 per cent efficient, a screen intensifier might improve fluoroscopic clarity if at the same time that it increases the brightness of the fluoroscopic image it allows the eye to operate more efficiently.

Physiologic studies indicate that the eye

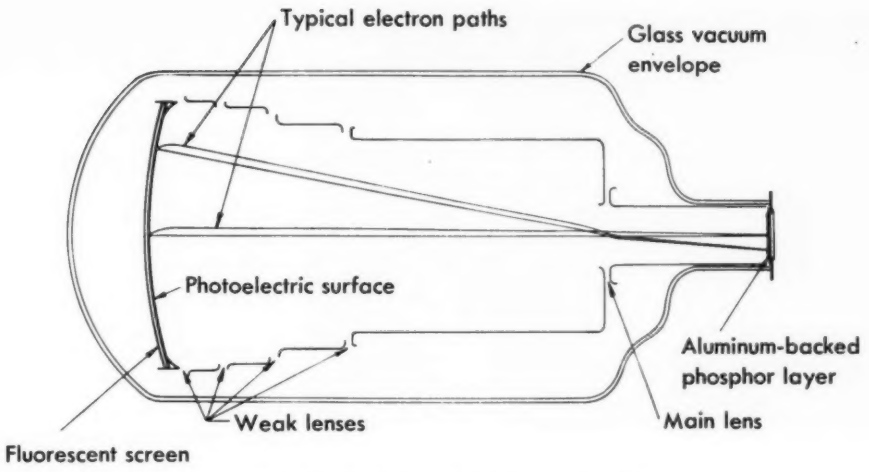


FIGURE 1. Schematic diagram of an x-ray image amplifier.

in conventional fluoroscopy actually does not operate very effectively.[7-9] Indeed, less than 5 per cent of the diagnostic information appearing in a fluoroscopic screen is recorded by the eye and transmitted to the brain. The low efficiency is principally due to the fact that only a small fraction of the light and therefore only a small part of the information emitted by the fluoroscopic screen are admitted to the eye of the observer under normal viewing conditions. Because of this, a considerable improvement in the clarity of fluoroscopy should be achieved by the introduction of a screen-intensification device if the instrument also improves the efficiency with which the information emitted by the screen is utilized. For example, an increase in efficiency from 2 to 100 per cent should cause an improvement in screen clarity equivalent to that produced by an increase in x-ray tube current from 5 to 250 ma. From experience, such an improvement is known to be substantial.

Methods of Screen Intensification

Image amplifiers—Although several methods have been developed to increase the brightness of fluoroscopic screens, one of the most successful is the electron optical intensifier[1,5] or image amplifier, shown schematically in figure 1. This instrument consists of an evacuated tubular glass envelope in which are located a conventional fluorescent screen at the left end of the tube and an aluminum-backed phosphor at the right end. The inner surface of the fluorescent screen is covered with a thin photoelectric layer, and between the screen and phosphor are placed many cylindrical electrodes which serve as electron lenses when suitable electric potentials are applied to the photoelectric layer, the electrodes and the phosphor.

The image amplifier operates in the following manner: Radiation from a conventional x-ray tube is projected through the patient and is allowed to impinge on the instrument's fluorescent screen. In response to the light generated by the screen, the photoelectric layer emits electrons having a spatial distribution proportional to the brightness of the screen; i.e., the fluorescent screen converts the x-ray image into a light image, and the photoelectric layer thereon creates a corresponding electron image. Electrons from the photoelectric layer are then accelerated down the length of the tube under the influence of the electric potentials applied to the cylindrical electrodes and fall on the phosphor at the tube's distal end. The impingement of the electrons on this phosphor produces a visible image which duplicates the pattern of that appearing on the x-ray fluorescent screen. However, due to the acceleration of the electrons

FIGURE 2. Image amplifier equipped with image Orthicon television system, operating in routine gastrointestinal fluoroscopy. Although the patient is in the lateral abdominal position, anatomic details are well seen.

within the tube, the brightness of the phosphor is many times greater than that of the x-ray fluorescent screen. The brightness is further increased by the fact that the size of the phosphor is small compared with that of the screen. The observer views the intensified image appearing on the phosphor by means of a telescopic eyepiece or other optical system to bring the size of the image back to normal perspective.

When image amplifiers were first introduced, they provided gains in screen brightness of about 500 times over conventional fluoroscopic screens. Also, their field of coverage was slightly less than 5 in. in diameter. More recently, image amplifiers having intensification factors providing as much as 3000 times the brightness of conventional screens have become available; the field of coverage has also increased to between 8 and 9 in. in diameter.

The efficiency with which image amplifiers utilize the diagnostic information contained in the x-ray beam is largely determined by the characteristics of the optical system which couples the amplifier to the observer's eye. Theoretically, this system can be designed to provide an efficiency closely approaching 100 per cent. As a result, image amplifiers are capable of yielding substantial improvements in fluoroscopic clarity. In practice, however, when highly efficient optical systems are employed, these instruments are quite difficult to use. Hence, with the image amplifiers available today, considerable optical efficiency is frequently sacrificed in order to achieve ease of operation. Unfortunately this has resulted in their clarity not being much greater than that of conventional screens. Also, operation is still often unsatisfactory because the observer's eyes must be kept in strict alignment with the optical system. This requirement obviously is difficult to maintain when several regions of a patient are to be examined.

Image amplifiers plus television systems—The recent adaptation of closed-circuit television systems to image amplifiers has greatly improved the usefulness of the latter.[3,4] In this application, a television camera is optically coupled to the image amplifier, and the observer views the intensified fluoroscopic image on a conventional television viewing tube. Such an arrangement is shown in figure 2. The patient is placed on a conventional fluoroscopic table with the x-ray tube below and the image amplifier above, in place of the conventional fluoroscopic screen. A television camera is attached to the image amplifier and converts the latter's image into an electric signal which, after amplification, is reconstructed on the face of the television viewing tube.

The added television system accomplishes several objectives. The observer is completely freed of the optical alignment problems of the simple image amplifier. Also, since the television system is capable of bringing the total

intensification of the fluoroscopic process to levels approximately 50,000 times those of conventional fluoroscopic screens, fluoroscopy can be conducted in daylight, even with the most difficult fluoroscopic projections. In addition, the television system permits many viewers to see the fluoroscopy simultaneously; hence, it is easy for the fluoroscopist to demonstrate his findings in a case to a colleague in consultation.

The efficiency with which information is utilized by image amplifiers equipped with television equipment is rather high, and therefore image clarity is quite good. Clarity is further improved by the fact that television systems increase the inherent contrast of fluoroscopic images and their detail is thereby enhanced.

Two types of television systems may be applied to image amplifiers. One is the so-called Vidicon system, which employs a Vidicon tube as the photosensitive element. The other is the so-called image Orthicon system, which uses an image Orthicon tube as the photosensitive element. The Vidicon system is inherently less sensitive than the image Orthicon, and at the present time is suitable only for fluoroscopy of children and of the adult chest. Even in the latter case, the Vidicon system must operate so close to its capacity limit that its performance is frequently something less than satisfactory. The image Orthicon system, however, has a sensitivity sufficient to permit daylight fluoroscopy even during the examination of heavy patients in the lateral lumbar projection. Image amplifiers equipped with image Orthicon television systems, therefore, provide the best screen intensification available today.

In spite of their apparent complexity, image amplifiers equipped with television systems are quite easy to use in practice. In fact, if the x-ray equipment is provided with an automatic x-ray intensity control, one is able to fluoroscope for several hours without attention to the equipment. Even when attention is required, the adjustments are simple and easily carried out. They are the same as those performed in the operation of a home television receiver.

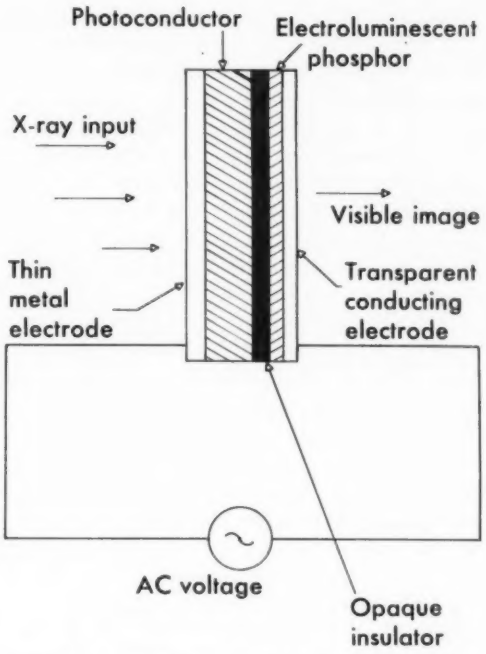


FIGURE 3. Schematic diagram of a developmental photoconductive-electroluminescent amplifier panel.

Photoconductive-electroluminescent panels—A great deal of work has been directed recently to the development of an entirely different type of screen-intensification system.[2] This device, shown schematically in cross section in figure 3, has much the appearance of a conventional fluoroscopic screen. The system consists of two principal elements: a photoconductive layer which intercepts the x-ray photons coming from the structure under examination and an electroluminescent layer which emits light when it is placed in an alternating electric field. The two layers are separated by a thin film of opaque material of high electric resistance. Also, a thin plate of conducting glass and a thin sheet of electrically conductive material such as aluminum are applied to the free surfaces of the electroluminescent and photoconductive layers, respectively. When the system is exposed to x-rays and a sinusoidal potential is applied to the aluminum and glass electrodes, a fluorescent image of the structure under examination

appears on the screen. The principles of operation are as follows: When x-rays are absorbed by the photoconductive layer, the layer's electric resistance decreases; hence, a greater fraction of the potential which prevails between the aluminum and glass electrodes appears across the electroluminescent layer. As a result, this layer emits light which may be seen by the observer through the glass electrode. Since the resistance of the photoconductive layer varies from place to place in accordance with the radiant intensity of the various x-ray images impressed on it, the electroluminescent layer exhibits a series of images which conform to the x-ray pattern.

Because of its relatively small size and simple construction, the photoconductive-electroluminescent intensifier has many potential advantages over image amplifiers either with or without television systems. However, in the present state of the engineering art, photoconductive-electroluminescent intensifiers are not practical instruments. Their brightness gains are small and their response is unusually slow. As a result, images smear badly when any motion is present. It appears that this characteristic is due to the rather poor mobility of the charges within the photoconductive and electroluminescent layers. Although it may be anticipated that this problem will be overcome, this type of screen intensifier is not yet suitable for fluoroscopic work.

Comment

This, then, is the state of the art in the field of x-ray screen intensification. Excellent instruments which brighten the fluoroscopic screen by as much as 50,000 times, without an increase in the x-ray dose rate to the patient, have become available. They provide substantial improvements in the fluoroscopic detail; eliminate entirely the need for dark adaptation; and, under such circumstances as fluoroscopy of children and of the adult chest, permit a reduction of the radiation dose rate as much as tenfold without serious loss of image clarity. Although they are rather costly and somewhat bulky, it may be confidently anticipated that both these problems will be resolved either by further developments in the image amplifiers and television systems currently available or through new instruments on which research is currently being vigorously pursued.

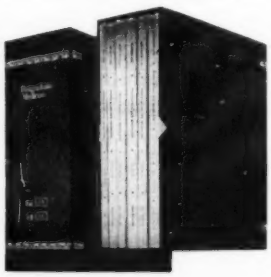
REFERENCES

1. Coltman, J. W.: Fluoroscopic image brightening by electronic means. Radiology 51:359, 1948.
2. Hadley, C. P. and Christensen, R. W.: Solid state image intensifier under dynamic operation. R.C.A. Rev. 20:670, 1959.
3. Morgan, R. H.: Screen intensification: A review of past and present research with an analysis of future development. Am. J. Roentgenol. 75:69, 1956.
4. ____: Development and state of x-ray television intensification in America. Proceedings of the Ninth International Congress of Radiology, Munich, 1959. (In press.)
5. Oosterkamp, W. J.: Image intensifier tubes. Acta radiol. (supp.) 116:497, 1954.
6. Chamberlain, W. E.: Fluoroscopes and fluoroscopy. Radiology 38:383, 1942.
7. Hecht, S.: Relation between visual acuity and illumination. J. Gen. Physiol. 11:255, 1928.
8. Hecht, S.: Quantum relations of vision. J. Optic Soc. America 32:42, 1942.
9. Rose, A.: Sensitivity performance of human eye on absolute scale. J. Optic Soc. America 38:196, 1948.
10. Sturm, R. E. and Morgan, R. H.: Screen intensification systems and their limitations. Am. J. Roentgenol. 62:617, 1949.

Your copies of

Postgraduate Medicine

are valuable



KEEP THEM FOR READY REFERENCE . . .

Custom-made for POSTGRADUATE MEDICINE, these binders will keep your copies clean, orderly and readily accessible for reference. Rich appearance of dark blue simulated leather cover and gold leaf embossed lettering make these binders a distinctive companion for your finest bindings. Gold foil provided for writing in volume number and year. Binders sent postpaid, carefully packed; 2 for $5.00, 4 for $9.50.

- Keeps current issues protected yet readily accessible
- Sturdy and attractive for your desk or library shelf
- Each binder holds one volume, 6 issues of POSTGRADUATE MEDICINE

ORDER FORM

POSTGRADUATE MEDICINE
Essex Bldg., Minneapolis 3, Minn.

2 Volume Binders $5.00 4 Volume Binders $9.50

Enclosed is $_____for_____binders to be sent postpaid

Name_____

Address_____

City_____Zone____State_____

...and how these differences can benefit your patients

particularly those with high cholesterol levels, coronary artery disease, and generalized atherosclerosis

MER/29 REDUCES CHOLESTEROL IN 8 OUT OF 10 PATIENTS: MER/29 reduces both serum and tissue cholesterol, *irrespective of diet.* Although some physicians prefer to use MER/29 in conjunction with controlled diets, cholesterol can be reduced successfully without such limitation.

CONCURRENT BENEFITS REPORTED IN SOME PATIENTS: In angina patients, some of the concurrent benefits reported include decreased incidence and severity of attacks, improved ECG patterns, diminished nitroglycerin dependence, and increased sense of well-being.

DIRECT, SPECIFIC CHOLESTEROL-LOWERING ACTION WITH MER/29: Some agents used to reduce cholesterol have other important primary effects — such as hormonal or vasodilator action. The primary, the *only* known function of MER/29 is to reduce cholesterol.

MER/29 HAS PRODUCED FEW SIDE EFFECTS, NO TOXICITY: Patients have been treated with MER/29 for continuous periods up to 19 months. In no case has there been evidence of serious toxic effects on the function of any vital organ or system. Side effects (nausea, headache, dermatitis) are rare and have usually been associated with dosages greater than those recommended for effective therapy. MER/29 is compatible with other cardiovascular therapies. It can be used along with measures which control anxiety, hypertension, obesity, and other conditions associated with cardiovascular disorders. These include nitroglycerin and PETN, and there have been no reports to date of incompatibility with anticoagulants.

CAUTION: Since long-term MER/29 therapy may be necessary, periodic examinations, including liver-function tests, are desirable. Also, since MER/29 inhibits cholesterol biosynthesis, and cholesterol plays an important role in the development of the fetus, the drug is contraindicated in pregnancy.

SUPPLIED: Bottles of 30 pearl gray capsules.

Complete bibliography and product information available on request.

MER/29

(triparanol)

Merrell SINCE 1828

The Wm. S. Merrell Company
Division of Richardson-Merrell Inc.
Cincinnati, Ohio • Weston, Ontario

Trademark: MER/29®

Medicine from Abroad

FROM POSTGRADUATE MEDICINE'S CORRESPONDENTS

ARGENTINA: ISAAC BERCONSKY, M.D.
AUSTRALIA: GRAYTON BROWN, M.D.
AUSTRIA: M. ARTHUR KLINE, M.D.
BRAZIL: A. BRICKMANN, M.D.
DENMARK: TORBEN JERSILD, M.D.
ENGLAND: R. SCOTT STEVENSON, M.D.
FINLAND: LEO NORO, M.D.
FRANCE: JEAN MEYER, M.D.
GREECE: NICK J. PHOTINOPOULOS, M.D.
ISRAEL: RAFAEL J. SCHEN, M.B.
JAPAN: HARUTO UCHINO, M.D.
SPAIN: MRS. EDITH BULSON

AUSTRALIA

High blood pressure in pregnancy—Dr. Lance Townsend, professor of obstetrics and gynaecology, University of Melbourne Faculty of Medicine, has reported on modern methods of treating high blood pressure during pregnancy in the *Medical Journal of Australia*. In order to ascertain the efficacy of current treatment, results obtained in a series of patients delivered in 1956 at the Royal Women's Hospital, Melbourne, were compared with those in a series delivered there in 1946 and 1947. The earlier series served as a control.

In 1946 and 1947, 8,069 patients were delivered at the Royal Women's Hospital. Of these, 111 (1.3 per cent) had high blood pressure. Of 6,866 patients delivered at this hospital in 1956, 109 (1.6 per cent) had high blood pressure.

During 1946 and 1947, most patients were ambulatory during treatment: there were comparatively few spare prenatal beds available, and these were reserved for patients with superimposed preeclampsia. No special attention was given to diet. When preeclampsia occurred (diagnosed by the appearance of protein in the urine) or when rise in blood pressure was excessive, the patient was admitted to the hospital. In the absence of proteinuria, the blood pressure usually dropped with bed rest, and, if the patient was not near term, she was discharged from the hospital. If she was near term, she remained in the hospital to await the onset of labor. If proteinuria was present, treatment consisted of bed rest and a low-protein diet with restricted fluid intake. If the proteinuria disappeared, the pregnancy was allowed to continue; if it persisted, labor was induced. This treatment conformed to that used in most of the world's obstetric centers at that time. Methods of treating high blood pressure began to change in 1950, and those currently in use gradually evolved.

In 1956, a gravida who had high blood pressure was admitted to the hospital for assessment of the cardiovascular system. After a few days of bed rest, her blood pressure usually dropped. She was then allowed to walk around the ward, and two or three days later a decision was made as to whether or not the use of hypotensive drugs was indicated. Any patient whose blood pressure

(Continued on page A-78)

anticholinergic
KEEPS THE STOMACH FREE OF PAIN

tranquilizer
KEEPS THE MIND OFF THE STOMACH

Milpath acts quickly to suppress pain and spasm, and to allay anxiety and tension with minimal side effects.

AVAILABLE IN TWO POTENCIES:

Milpath-400 — Yellow, scored tablets of 400 mg. Miltown (meprobamate) and 25 mg. tridihexethyl chloride. Bottle of 50.

Dosage: 1 tablet t.i.d. at mealtime and 2 at bedtime.

Milpath-200 — Yellow, coated tablets of 200 mg. Miltown (meprobamate) and 25 mg. tridihexethyl chloride. Bottle of 50.

Dosage: 1 or 2 tablets t.i.d. at mealtime and 2 at bedtime.

Milpath®

®Miltown + *anticholinergic*

WALLACE LABORATORIES *Cranbury, N. J.*

during recumbency was 150/90 mm. of mercury or above was immediately treated with hypotensive drugs. Sixty-eight of the 109 patients in the series studied by the author were given SERPASIL® in the first trimester. This drug rarely causes orthostatic hypotension, and it can be used with other hypotensive drugs, especially the ganglion-blocking agents. After some days of in-hospital treatment with hypotensive drugs, the patient's blood pressure usually dropped below 150/90 mm. of mercury and she was discharged to the prenatal clinic.

A regular check was made of weight gain during pregnancy. If the patient's initial weight was more than 140 lb., a protein-rich reducing diet of low sodium content was prescribed from the beginning of pregnancy. If her initial weight was less than 140 lb., the usual diet for pregnancy was allowed, excluding added salt at meals. This diet contained 3000 calories per day.

In many patients, including some who were receiving Serpasil, the blood pressure tended to rise during or about the twenty-fourth week of pregnancy. If the patient had not been given Serpasil, it was then administered to her. For many who were already taking this drug, administration of the ganglion-blocking agent ANSOLYSEN® was used to control blood pressure.

The immediate prognosis for the patients in both series was good. There were no maternal deaths in the 1956 series and only one in the 1946 and 1947 series. However, the later prognosis might have been less favorable if there had been any residual elevation in blood pressure post partum.

Statistical analysis showed that there was a highly significant reduction in the number of therapeutic abortions and in perinatal mortality in the 1956 series in comparison with the earlier one. In the 1946 and 1947 series the perinatal mortality was 11 per cent. The fetal wastage was nil in the 1956 series when the diastolic blood pressure was kept below 90 mm. of mercury during pregnancy. Thus, to ensure a successful pregnancy, it would seem that therapy should be directed toward keeping the blood pressure below this level.

The important changes made by 1956 in the treatment of hypertension in pregnancy were regular prenatal visits, control of weight gain with a high-protein reducing diet, restriction of sodium chloride intake, immediate admission to the hospital for rest if required, and the use of hypotensive drugs.

BRAZIL

Malnutrition in civilian and military populations—In a report in *Arquivos brasileiros de nutrição*, H. V. Alves Mauricio has cited the frequency of malnutrition in Brazil. Malnutrition was considered the main cause of unfitness for military service in 52 per cent of those joining the army and in 30 per cent of those entering the navy. The incidence of malnutrition is higher in the north and northwestern regions of the country.

The author called attention to the way in which the armed forces contribute to re-establishment of good nutrition by providing an ample, balanced diet and by education on nutrition.

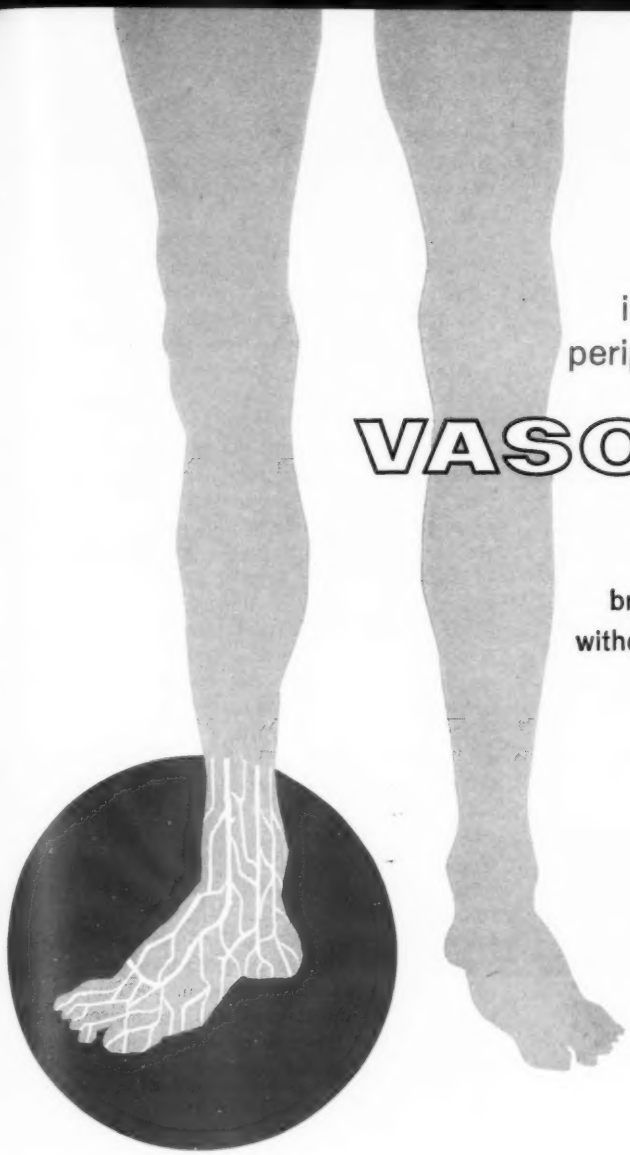
Cancer of the tongue and floor of the mouth—In *Revista paulista de medicina*, J. F. Barbosa has presented the results of a study of 445 patients with cancer of the tongue or floor of the mouth, or both, who were seen at the Instituto Central of the Associação Paulista de Combate ao Câncer from July 1953 to December 1958, inclusive.

Only 198 of the 445 patients were included in the follow-up study; the other 55 per cent were not included because the disease was too far advanced or because they either would not accept treatment or received only palliative therapy. In 67 of the patients studied, the primary lesions were treated by surgery; radiation was used in 153 patients. In 22 of the patients treated surgically, radiation had been employed but had not been effective. Seventy-five per cent of the primary lesions treated by surgery were arrested for at least one year, and growth was stopped in 50.8 per cent of those treated by radiation. The prognosis for patients undergoing surgery was worse than that for those who received radiation.

Up to the time of this study, radiation was the treatment of choice for cancer of the tongue and floor of the mouth at the Instituto Central. However, results of this study led to a change in procedure; now, surgery and roentgentherapy are equally considered for patients with early or advanced stages of the disease.

The author recommends the following surgical procedures.

(Continued on page A-80)



in diabetic patients with peripheral vascular disease

VASODILAN®

Isoxsuprine hydrochloride, Mead Johnson

myo- -vascular relaxant

brings blood to deep tissues— without affecting diabetes control[1,2]

- provides relief in a high percentage of patients with a wide variety of peripheral vascular disorders[2-8]
- effective in intermittent claudication,[3,4] coldness and numbness of extremities,[6] trophic ulcers,[7] and leg cramps[5,6,8] associated with arteriosclerosis obliterans, diabetic vascular disease, Buerger's disease, Raynaud's disease and frostbite
- may be used in controlled diabetics without effects on blood sugar levels, insulin or tolbutamide requirements[1,2]
- increases blood flow by direct action on the smooth muscle of the blood vessels[2,3]

dosage: 1 or 2 tablets (10 to 20 mg.) three or four times daily.

supplied: 10 mg. tablets, bottles of 100; 2 cc. ampuls (5 mg./cc.) for intramuscular use, boxes of 6.

references: (1) Samuels, S. S., and Shaftel, H. E.: Effects of Isoxsuprine Hydrochloride on Blood Sugar Levels and on Requirement for Insulin or for Tolbutamide in Normal Subjects and in Diabetic Patients, to be published. (2) Samuels, S. S., and Shaftel, H. E.: J.A.M.A. *171*:142-144 (Sept. 12) 1959. (3) Kaindl, F., *et al.*: Angiology *10*:185-192 (August) 1959. (4) Kraucher, G.: Prakt. Arzt *11*:325-329 (May) 1957. (5) Birkmayer, W., and Mentasti, M.: Wien. med. Wchnschr. *108*:395-396 (May 3) 1958. (6) Clarkson, I., and LePere, D.: Angiology *11*:190-192 (June) 1960. (7) Billiottet, J., and Ferrand, J.: Sem. méd. *34*:635-637 (May) 1958. (8) Singer, R.: Wien. med. Wchnschr. *107*:734-736 (Sept.) 1957.

Mead Johnson

Symbol of service in medicine

11460

1. Partial excision of the tongue or floor of the mouth for lesions in the early stage.

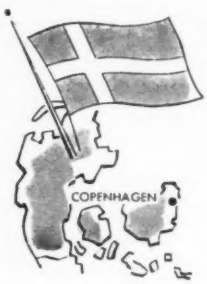
2. Hemiglossectomy or excision of half of the floor of the mouth for more advanced lesions which do not overlap the raphe of the tongue. Neck dissection using the en bloc principle of the pull-through procedure is always employed in these operations.

3. The pull-through or "commando" procedure for lesions which have invaded the alveolar border, depending on the degree of invasion of the bone.

4. En bloc removal of lesions of the central part of the base of the tongue, with bilateral neck dissection by means of transverse pharyngectomy.

In the author's opinion, roentgentherapy is the treatment of choice for (1) patients with very advanced stages of the disease in whom total or subtotal glossectomy would be required to remove the tumor; (2) patients whose general condition is poor and who could not withstand surgery; (3) patients who will not accept surgical treatment, and (4) patients for whom only palliative treatment can be given.

DENMARK



Infantile spasms and hypsarrhythmia—Erna Christensen and Johannes C. Melchior have presented six autopsy reports on children with infantile spasms and hypsarrhythmia. The pathologic anatomic findings included endogenous and exogenous changes and transitional cases. The typical findings in all patients were degenerative or dysplastic alterations in the cortex. The authors believe that infantile spasms and hypsarrhythmia depend on the degree of maturation of the nervous system, especially of the ganglion cells, and on the patient's age. The syndrome can only be seen when there is a discrepancy between these two factors.

Efficacy of silver nitrate in eyes of newborn—H. H. Seedorff has described an experiment carried out in two similar maternity departments to determine the efficacy of silver nitrate in the eyes of the newborn. In one department, no prophylactic agent was used, while in the other department all infants received the usual treatment with silver nitrate. In the untreated group, seven cases of gonococcal ophthalmoblennorrhea and 80 cases of nonspecific conjunctival infections occurred. In the other group, there were no cases of gonococcal ophthalmoblennorrhea and only nine cases of nonspecific conjunctival infections. Sensitivity tests were performed on the bacterial cultures.

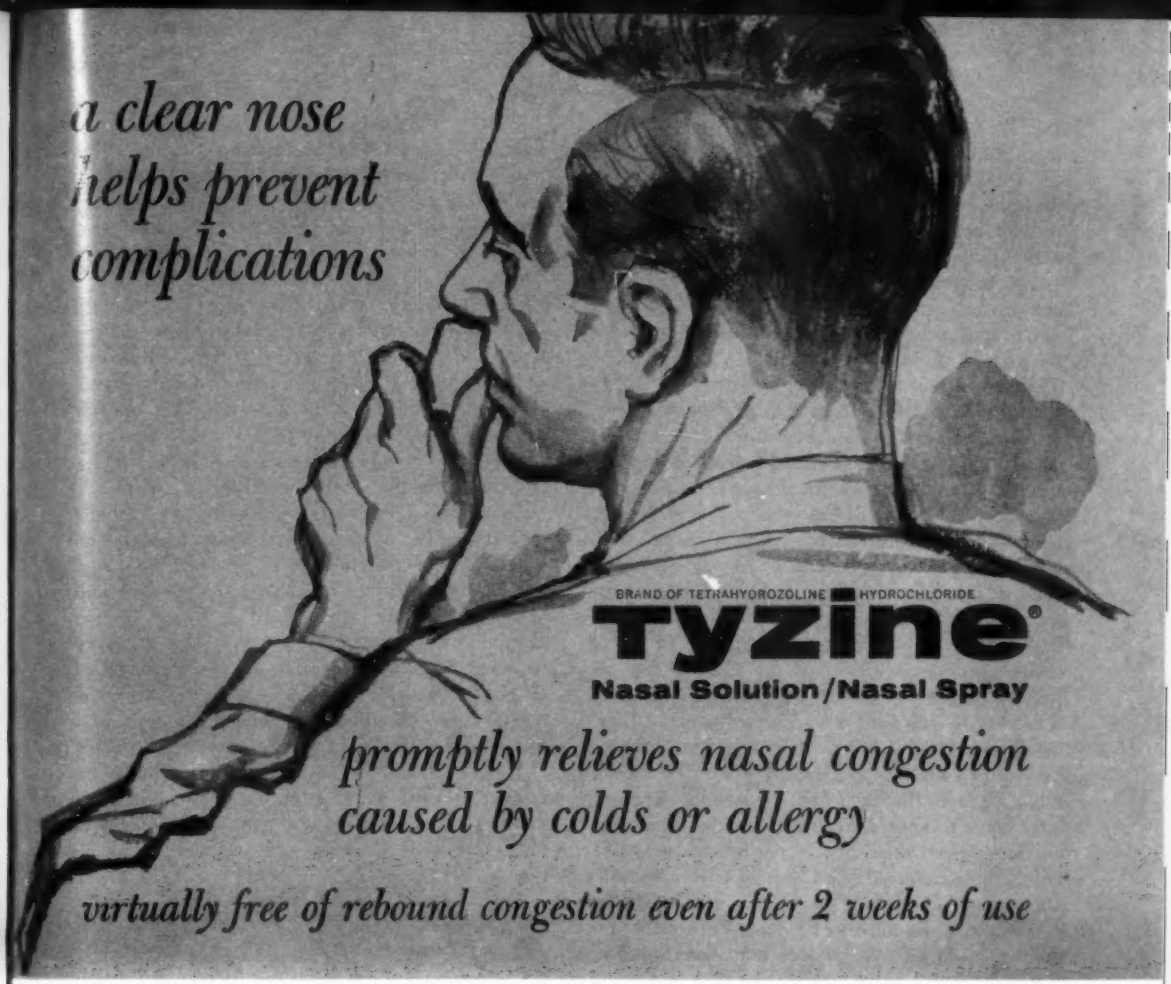
Allergic reaction to poliomyelitis vaccine—Axel Klee has reported on a 31 year old woman in whom neurologic complications developed within hours after she had received her fourth vaccination against poliomyelitis. The complications included headache, stiffness of the neck, fever, double vision, vertigo, clouding of consciousness, difficulty in walking, and weakness and ataxia, particularly in the left limbs. Repeated lumbar punctures showed a slight increase in the level of protein in the cerebrospinal fluid. There was a gradual improvement during a period of five to six months, but a second attack localized to the lower motor neurons occurred following a febrile episode. Symptoms referable to the brain stem and diffuse reduction of tone and power, particularly on the left side, were present. Electromyography revealed evidence of polyneuritis. Since a cerebral tumor was suspected, air encephalography and vertebral angiography were performed, but both tests gave negative results. Attempts to culture poliomyelitis virus from the feces and spinal fluid were unsuccessful. After several months, the patient recovered gradually from the second attack.

The author cited literature on the neurologic sequelae of serum therapy and vaccination, and concluded that this was probably a case of allergic reaction to the injection of poliomyelitis vaccine.

ENGLAND

Cholangiography—At a discussion on this subject at the Royal Society of Medicine, Professor A. G. R. Lowdon, of Newcastle upon Tyne, said that after an early phase of great expectations, he has found intravenous and oral cholangiography of limited value. The significance of a dilated duct is not always clear—

(Continued on page A-82)



IN BRIEF

TYZINE is tetrahydrozoline hydrochloride, a sympathomimetic amine with potent decongestant properties. Relief is almost immediate and lasts four to six hours after a single administration. Virtually free of sting or burn and rebound congestion . . . odorless and tasteless. TYZINE is not significantly absorbed systemically when used as directed . . . does not impair ciliary activity . . . and is physiologically buffered to pH 5.5.

INDICATIONS: Relieves inflammatory hyperemia and edema of the nasal mucosa and congestive obstruction of sinus and eustachian ostia, as may occur in the common cold, hay fever, perennial vasomotor rhinitis, chronic hypertrophic rhinitis, and sinusitis.

DOSAGE AND ADMINISTRATION: Adults and Children 6 Years and Over—2 to 4 drops of TYZINE (0.1%) in each nostril as needed, not more often than every three hours. When using TYZINE Nasal Spray, insert tip of plastic bottle into nostril, tilt the head slightly forward from an upright position, and squeeze sharply 3 or 4 times, not more often than every three hours.

Important: Use TYZINE Pediatric Nasal Drops (0.05%) for children under 6 years. The 0.1% concentration is contraindicated in this age group.

SIDE EFFECTS: Transient mild local irritation after instillation has been reported in rare instances.

PRECAUTIONS: Avoid doses greater or more frequent than those recommended above. Use with caution in hypertensive and hyperthyroid patients.

Overdosage may cause drowsiness, deep sleep, and, rarely, marked hypotension in infants and young children. KEEP OUT OF HANDS OF CHILDREN OF ALL AGES.

SUPPLIED: *Nasal Solution,* 1-oz. dropper bottles, 0.1%. *Nasal Spray,* 15 cc., in plastic bottles, 0.1%. *Pediatric Nasal Drops,* ½-oz. bottles, 0.05%, with *calibrated* dropper.

More detailed professional information available on request.

Science for the world's well-being™ Pfizer PFIZER LABORATORIES *Division, Chas. Pfizer & Co., Inc. Brooklyn 6, New York*

it might suggest present or previous obstruction by stone, but sometimes it is the result of other diseases, such as chronic pancreatitis, fibrosis of the sphincter of Oddi, or dyskinesia. Operative cholangiography has been practiced for so many years that it is surprising to find that the surgical profession still seems undecided or divided about its value. It is not used routinely except by a small number of surgeons in this country. This might mean that it is not worth doing. On the other hand, if we think that it is worth doing, we must be prompted to ask why the measure is so unpopular. The answer, doubtless, is that the technic is, or appears to be, time consuming, and that until the drill has been practiced to perfection many frustrating mistakes will occur. Bad pictures mean repeating the whole process or accepting the fact that time and effort have been wasted.

Apart from using cholangiography to avoid unnecessary exploration of the duct, it has its important uses as a supplement to, rather than a substitute for, careful surgery. Professor Lowdon has found it invaluable as a postexploratory measure to make sure that all stones have been removed from the duct. Most, if not all, surgeons have come to accept the fact that a postoperative cholangiogram should be made through a T tube before it is removed. Surely it is only a reasonable extension of thought to conclude that this examination should also be made before the abdomen is closed. On more than one occasion Professor Lowdon has avoided leaving stones behind with the aid of operative cholangiography.

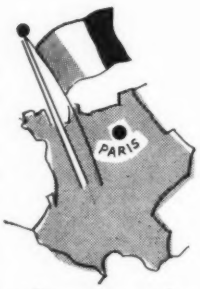
Leukemia and radiation—Interest in the effects of small doses of ionizing radiations has focused attention on the possibility that doses of x-rays such as are used in medical diagnostic radiology may on occasion be carcinogenic. However, published data on the leukemogenic effect of irradiation in utero are conflicting. Under the direction of the Medical Research Council, Dr. W. M. Court Brown, Edinburgh, and Drs. R. Doll and A. Bradford Hill, well-known medical statisticians, investigated the incidence of leukemia after exposure to diagnostic radiation in utero. Eight hospitals were selected, four in Edinburgh and four in northwest London, and the results of this study have been published in the *British Medical Journal.*

Evidence of the leukemogenic effect on the fetus of exposure to ionizing radiations in utero was sought by comparing the mortality rate from leukemia in children whose mothers were known to have had irradiation during pregnancy with that expected from the corresponding sex and age-specific national mortality rates. Pregnant women who received diagnostic irradiation directed toward the abdomen or pelvis between 1945 and 1956 were identified in the records of the radiologic departments of the eight hospitals in London and Edinburgh. Information about the date of birth and sex of the child was obtained from the corresponding maternity records. If the child left the hospital alive, his full name and the first name of his father were obtained from the local register or, in a few instances, from the Central Register of Births.

Information was obtained on 39,166 liveborn children whose mothers were known to have had abdominal or pelvic irradiation during pregnancy. Among these children, nine died of leukemia before the end of 1958. The expected number was estimated to be 10.5. There was no evidence of any disproportionate occurrence of leukemia among the children who had been the most heavily irradiated or among children who had been irradiated early in intrauterine life.

It was concluded that an increase of leukemia among children due to radiographic examination of the mother's abdomen during pregnancy was not established.

FRANCE



Gout—In *La Presse médicale,* Professor De Seze has reported on his study of more than 300 patients with gout. Good results were obtained in 60 per cent of 160 patients who received colchicine orally during acute gouty attacks. The remaining patients had to discontinue using colchicine because of digestive disturbances and diarrhea with exsiccation. The agent was administered intravenously in 24 patients, but the author determined that this method should not be used because of the danger of local inflammatory reaction. Prolonged treatment with colchicine (1 mg. daily for one to three years) was effective and well tolerated in 11 of 14 patients, but it did not reduce the overload of urates.

Although phenylbutazone produced good results in 81 per cent of 110 patients, there were

(Continued on page A-84)

...the proof of the Patrician "200" is in the radiograph!

When you choose x-ray for private practice, look at performance as well as the price tag. "Economy" that is gained by short-cuts in table design or a reduction in power may mean slow exposures, blurred radiographs and repeated retakes. General Electric's Patrician "200" combination is designed with adequate power for private practice — a full 200 ma to stop anatomical movement sharply and clearly. Many other features found in larger installations are engineered into the Patrician: 81" table, independent tubestand, shutter limiting and automatic tube protection, to name just a few. And, considering its *uncompromising* G-E quality, this Patrician "package" is remarkably low priced.

Rent the Patrician through the G-E Maxiservice® plan that provides the complete installation, *including* maintenance, parts, tubes, insurance, local taxes — *everything* in one monthly fee. Get details from your G-E x-ray representative or mail coupon.

Progress Is Our Most Important Product

GENERAL ELECTRIC

General Electric X-Ray Department
Milwaukee 1, Wisconsin, Room D-21

Send me: ☐ Patrician bulletin
☐ Maxiservice bulletin

Name_____

Address_____

_____

many untoward effects, including edema caused by retention of sodium, gastric disturbances, bleeding from the intestinal tract, and colicky kidney pains. Professor De Seze suggested that phenylbutazone be administered only to those patients who cannot tolerate colchicine.

Corticosteroids such as prednisone are not effective in treating gout unless the dosage is at least 40 mg. Prednisone gives good results and is well tolerated; it does not cause digestive disturbances. When the dosage is reduced, 1 mg. of colchicine given daily should be added to the regimen.

Cinchophen is only moderately effective and colchicoside is of little value in treating gout. Aspirin in a dosage of 4 to 5 gm. per day produced good results in only 22 of 180 patients studied by Professor De Seze; however, it proved useful as a supplementary medication.

An intolerance to probenecid developed in 43 of 126 patients who received this drug. Although good results were obtained with probenecid, it had to be supplemented with colchicine or phenylbutazone from the beginning of treatment. The author concluded that salicylates must be avoided, because they are not easily handled and are less effective when used for prolonged periods. Zoxazolamine, in a dosage of 125 mg. three times a day for several months, was well tolerated but requires further study for accurate evaluation.

The basic treatment of gout is control of diet. It was observed that gouty attacks were rare during wartime dietary restrictions. The intake of proteins, lipids, calories and substances which might increase the level of uric acid in the blood should be reduced, and alcoholic beverages should be prohibited.

Dr. Claude Bourde, Marseilles Hospital, has described vascular accidents caused by gout in *Angéiologie et annales de la Société française d'angéiologie et d'histopathologie.* He observed 15 patients with arterial obstructions in the tibialis anterior and the dorsalis pedis arteries. Such accidents may occur either in known cases of gout or as the first symptoms of gout.

The manifestations of gouty arteritis are pain and inflammation of the dorsum of the foot and local edema of the limbs. Oscillometric study of the affected limbs reveals sharp oscillations of a paradoxical nature (Mathieu's phenomenon) which are of great value in diagnosis. The level of uric acid in the blood is high, but it usually decreases during an attack of gout. Colchicine and phenylbutazone produce a sedative effect in such cases, while vasodilators aggravate the symptoms and may even cause gangrene. Roentgenographic examination shows bony changes, and arteriography indicates normal arterial calibers except in the obstructed area. The irregularities and segmental lesions typical of Buerger's disease are absent. Two complications which can occur are gouty phlebitis with cyanosis (phlegmasia cerulea dolens) and erythromelalgia.

It is possible that a systematic measurement of uric acid would indicate that more than half of the patients with arteritis have gout. Current clinical medicine attributes too much importance to the increased level of cholesterol in the blood, while neglecting the importance of gout.

ISRAEL

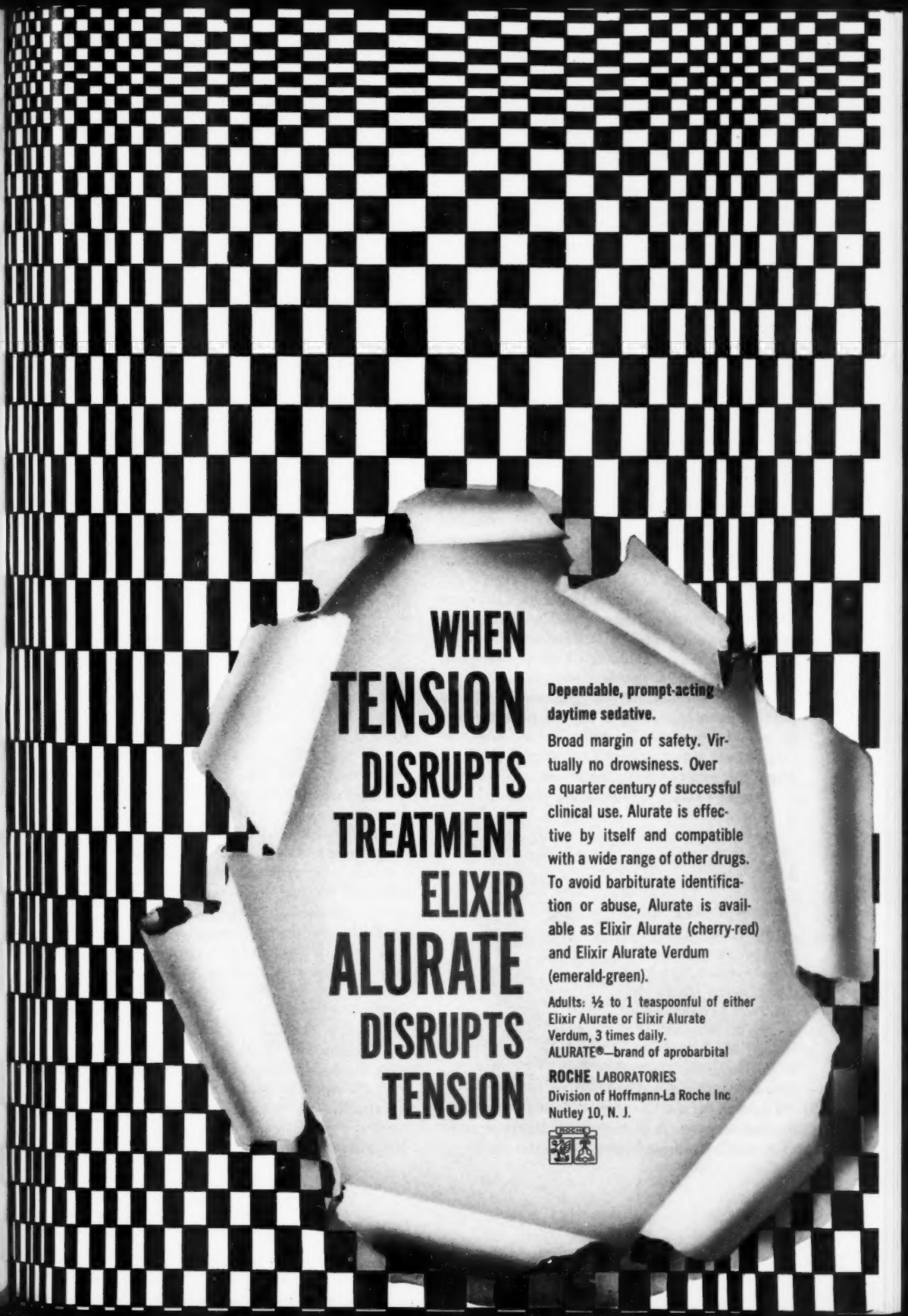
Leptospirosis—A survey of the incidence of leptospirosis in Israel from 1949 to 1957 has been reported by Z. Cochavy in the *Israel Medical Journal.* In 1949 and 1950, a severe epidemic occurred in the southern coastal plain area, which is extensively cultivated and irrigated. The majority of patients were agricultural workers who had become infected with *Leptospira grippotyphosa.* The source of infection was thought to be the vole (field mouse).

Since 1951, the incidence of the disease has diminished greatly, with approximately 30 cases reported each year. However, leptospirosis remains a potential danger to agricultural workers, since both *L. grippotyphosa* and *L. canicola* have been found in cattle and other farm animals inhabiting the southern coastal plain.

Infection with *L. icterohaemorrhagiae* is rare in Israel; only eight cases were reported during the eight year period studied. These cases occurred in the port areas of Haifa and Tel Aviv, where rats presumably were the carriers of infection.

Acute erythremia—A. Zlotnick has discussed a case of DiGuglielmo's disease (acute erythremia) in the *Israel Medical Journal.* This disease is characterized by a general proliferation of erythrocytopoietic cells located in the bone marrow.

(Continued on page A-86)


WHEN
TENSION
DISRUPTS
TREATMENT
ELIXIR
ALURATE
DISRUPTS
TENSION
Dependable, prompt-acting daytime sedative.
Broad margin of safety. Virtually no drowsiness. Over a quarter century of successful clinical use. Alurate is effective by itself and compatible with a wide range of other drugs. To avoid barbiturate identification or abuse, Alurate is available as Elixir Alurate (cherry-red) and Elixir Alurate Verdum (emerald-green).
Adults: ½ to 1 teaspoonful of either Elixir Alurate or Elixir Alurate Verdum, 3 times daily.
ALURATE®—brand of aprobarbital
ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc
Nutley 10, N. J.

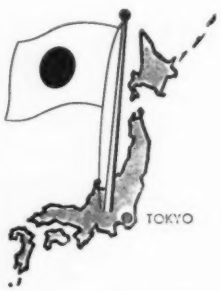
The patient was a 72 year old woman who had severe anemia, with a hemoglobin of 4.8 gm. Many erythroblasts, often abnormal in appearance, were found in the peripheral blood. Leukopenia was present at first but later the white blood cell count rose to 12,600, with a ratio of 163 erythroblasts to every hundred white blood cells. A bone-marrow aspirate showed hypercellularity in the erythrocytic series. The large number of plasma cells present probably was associated with the 31.6 per cent level of gammaglobulin. Tissue mast cells also were numerous in this patient.

The disease ran a fulminant course of seven weeks, with a fatal outcome.

Q fever as a cause of hepatitis—In *Harefuah*, W. J. Elkan and C. Bechar, Zrifin Government Hospital, have described a case of fever marked by transient icterus and pain in the region of the liver. Complement-fixation tests for *Rickettsia burnetii* showed a titer of 1:60, which later rose to 1:320. Treatment with chloramphenicol effected an immediate drop in the patient's temperature and resulted in full clinical recovery.

Following this experience, the authors conducted routine tests for Q fever in all cases of acute hepatitis encountered during a two year period. Five additional patients with high complement-fixation titers for *R. burnetii* were seen. Positive results of tests of liver function were obtained in these patients, and their clinical pictures were typical of infectious hepatitis. In one case, serologic tests were performed on cows on the farm where the patient lived; results showed that five of nine cows had agglutinating antibodies for *R. burnetii*.

JAPAN



"Air-pocket" phenomenon—An entity termed the air-pocket phenomenon has been described by Dr. F. Matsunaga, professor of medicine, Hirosaki University Medical School, in the *Japanese Journal of Gastroenterology*. Dr. Matsunaga defined the phenomenon as a decrease in skin temperature at the paravertebral segment of viscera, which indicates diseased viscera according to the distribution of spinal cord segmentation. This sign is one of the viscerovegetative nerve reflexes occurring from the relation between the interoceptive fibers in the visceral nerves and the sympathetic nerves in the spinal cord itself, and it is thought to be useful in both diagnosis and treatment.

In order to measure the decrease in skin temperature accurately, Dr. Matsunaga developed an improved pyrometer which he has named the Dermatothermograph, using a thermister with an automatic balancing electron tube.

In the series of patients studied, the air-pocket phenomenon was observed in all patients with pleurisy; in 91 per cent with heart disease; in more than 80 per cent with disorders of the bile duct, stomach and duodenum (particularly in those with peptic ulcer), and in 78 per cent with pulmonary tuberculosis.

Dr. Matsunaga pointed out that his method provided results differing from those reported previously. This was noted particularly in diseases of the upper gastrointestinal tract, in which the air-pocket phenomenon was seen not only in the middle thoracic segment but also in the upper and lower thoracic segments, and in diseases of the intrathoracic organs and in renal diseases, in which the phenomenon was observed in both the upper thoracic and the lower cervical segments.

Treatment of leukemia—At the eighth meeting of the International Congress of Hematology in Tokyo, Dr. Susumu Hibino, professor of medicine, Nagoya Medical College, discussed his experiences with the new chemotherapeutic agents for treating leukemia which have been discovered recently in Japan, including mitomycin C, T431-L and RC-4.

In chronic leukemia, it was demonstrated that mitomycin C reduces the number of leukemic cells and the size of an enlarged spleen to a degree comparable to that produced by busulphan or triethylenethiophosphoramide. Following treatment with mitomycin C, no cases of acute myeloblastic transformation were seen. RC-4 also is as effective as the conventional alkylating agents in treating leukemia.

In acute leukemia, the combination of 6-mercaptopurine and T431-L produced the best results in terms of the rate and duration of remission. A study is being made of the effects of treatment with a combination of 6-mercaptopurine, prednisolone, mitomycin C and T431-L, but the results are not yet conclusive.

Nutrition in Relation to Arteriosclerosis

FREDRICK J. STARE*

Harvard University School of Public Health, Boston

Since arteriosclerosis is now regarded as a metabolic disorder, nutrition is considered one of the important factors in its development, treatment and prevention.

Experimental production of atherosclerosis has been concomitant with production of high serum cholesterol levels.

Saturated fats in the diet increase serum cholesterol, while polyunsaturated fats reduce it.

The author believes that the total caloric intake is the most important influence on serum cholesterol.

Dietary modifications are suggested which will reduce the caloric intake of fat.

FREDRICK J. STARE

In the past decade, research on the causes, treatment and possible prevention of arteriosclerosis has expanded greatly. Only a decade ago arteriosclerosis was usually thought of as a degenerative disease, and there was little hope that its course could be affected; today, it is generally regarded as a metabolic disorder. Hopes are high for improved treatment and prevention in the sense that its onset may certainly be postponed.

Much of this research and this new hope involves various aspects of the science of nutrition. This has come about for a number of reasons, among which are the following:

1. About 1950, it was observed that vegetarians have appreciably lower serum cholesterol levels and a lower incidence of coronary disease.

2. It has been observed that coronary infarction is less likely to develop in persons with lower serum cholesterol levels.

3. Epidemiologic observations in many parts of the world have indicated that groups of people who consume little fat in the diet are less apt to have coronary disease. In many areas of the world, coronary infarction is a rare disorder.

4. A number of studies on various formula feedings which were begun seven or eight

*Professor, Department of Nutrition, Harvard University School of Public Health, Boston, Massachusetts.

Presented before the forty-fifth annual Assembly of the Interstate Postgraduate Medical Association at Pittsburgh.

years ago and are continuing today show that those formulas in which saturated fats predominate elevate the serum cholesterol level, while those which are rich in polyunsaturated fats reduce this level. I would like to interject here that I am not at all sure that the results of these studies, which are highly experimental, apply to our eating meat and potatoes. Nevertheless, these studies have served to stimulate considerable interest in the possible effect of fat and types of fat on the serum cholesterol level.

5. It has been shown in a number of laboratories that a rapid gain in weight is one of the factors which seem to cause or are accompanied by an elevated serum cholesterol.

6. We all are aware of the classic studies of Dr. Timothy O'Leary in Boston, who produced atherosclerosis in rabbits a generation ago. In the last 10 years, atherosclerosis has been produced experimentally in at least six or seven other species, including the chicken, dog, monkey, rat and guinea pig. Interestingly, the experimental production of atherosclerosis has been possible only when an elevation of serum cholesterol has been achieved.

In regard to the experimental production of atherosclerosis and to nutrition in atherosclerosis, I would like to point out that many components of nutrition are involved. These include protein, type of carbohydrate, choline and pyridoxine. It is not simply a question of the fat and the type of fat in the diet, even though these are important considerations.

In this discussion, I will limit my comments to a few points on nutrition which may have some practical importance. The studies which will be discussed were done in our own laboratory with a number of my colleagues, and most of them have been published.

In a study we reported about five years ago in the *American Journal of Medicine*, we computed the average cholesterol level for almost 2000 healthy men who had no evidence of cardiovascular disease. We also found the average serum cholesterol level for a group of 273 men who had had definite myocardial infarctions. The figure for the latter group was considerably higher. An elevation in serum cholesterol seems especially significant in persons who have not yet reached the 55 to 60 year age range. We had somewhat over 300 well men at age 45 whose cholesterol levels averaged around 240 mg. per cent, and we had approximately 70 men in that age group who had had infarctions and whose cholesterol levels averaged about 280 mg. per cent.

Effect of Caloric Intake on Serum Cholesterol

Now, what influences the serum cholesterol level? In my opinion, perhaps the most important influence is not necessarily the type of fat or the type of carbohydrate in the diet, but rather the total caloric intake. However, some experimental studies indicate that the type of carbohydrate is important and conceivably may be just as important as the type of fat.

In a study done a few years ago, we showed how it is possible for a marked gain in weight to influence the serum cholesterol level, even though that increase comes purely from an excess of sucrose. This experiment involved a 27 year old man whom we studied for three months. During the first month, his diet consisted of 3000 calories daily. He maintained his body weight on this intake, and his serum cholesterol level was 125 mg. per cent. At the start of the second month, we increased his dietary intake by 2000 calories, to a total of 5000. The extra 2000 calories consisted exclusively of sucrose. It was a highly artificial diet, and in order to ingest those additional calories he had to drink such things as KARO® syrup and soft drinks with a great deal of added sugar. The diet was exceedingly low in fat (less than 15 gm. daily) and in cholesterol (less than 50 mg. daily). During this second month, with the extra 2000 calories per day, the man gained 11 lb., and his cholesterol level went up to 200 mg. per cent. For the third month, we put him back on 3000 calories daily. He lost 8 lb., and his cholesterol level decreased, but not to its former level.

When we had completed this study, we wondered what would have happened if we could have prevented the subject's weight gain by means of forced exercise. In other words, if he had burned up those extra calories by

hard physical work, would his serum cholesterol level still have increased? When we undertook to answer this question, we made a change in the diet. We decided to load the experiment in favor of the development of cholesterol. Thus, we made the diet very high in fats by increasing the fat constituent to 175 gm. and the cholesterol to 2000 mg.

During the first month of this second period, we gave our subject 3000 calories per day and required no unusual exercise of him. His weight was 196 lb., and his cholesterol was 155 mg. per cent. During the second month, we got him to consume over 6000 calories and to perform about seven or eight hours of very hard exercise daily. He gained only 4 lb. despite his tremendous caloric intake, and there was no appreciable change in his serum cholesterol level (165 compared with 155 mg. per cent). The exercise was eliminated during the third month. Without exercising, the subject found that he just could not consume 6000 calories daily. He did manage an intake of 5400 calories, however, and in that single month he gained 14 lb., or almost ½ lb. per day. His cholesterol level rose to 275 mg. per cent. In the last period, we decreased his diet to 2300 calories; he lost 8 lb., and his cholesterol level was on the way down.

I think these experiments illustrate that for some individuals a rapid gain in weight is accompanied by an increase in serum cholesterol. Almost regardless of the fat content of the diet, if one does not gain weight (either by keeping the caloric intake low or by burning up the extra calories through exercise), the chances of an increase in serum cholesterol are rather slight.

Dietary Modifications

Now, I want to discuss some diets and point out their respective caloric content. In a typical American diet, we get somewhere in the neighborhood of 40 per cent of our calories from fats. Of that 40 per cent, a little less than half (around 18 per cent of the total caloric content) comes from what we call the saturated fatty acids, which for all practical purposes are from dairy and meat fats. About the same proportion (18 or 19 per cent of the total caloric intake) comes from what we call the monounsaturated fats, which for all practical purposes are from meat fats, shortenings and margarines. Somewhere around 4 to 5 per cent of our calories comes from what we call the polyunsaturated fats, mainly from corn, cottonseed or soybean oil, used as such in salad oils or used partially hydrogenated, as in most margarines and shortenings.

As the result of a great deal of experimentation and some epidemiologic and clinical studies during the past 10 years, many workers in this field think it desirable for the American public to reduce modestly its consumption of fats. Now, there is considerable difference between reducing and eliminating the consumption of fats. It is ridiculous to talk about eliminating fats from the diet, and I think it is equally ridiculous to talk about cutting the fat constituent in half, because, if dietary regulations are to be any good, they must be such that people can follow them willingly. A 25 per cent reduction in total fat, so that somewhere around 30 per cent of our total calories would come from fats, constitutes a modest reduction.

There is some indication that an increase in the polyunsaturated fats is desirable, because as cholesterol esterifies in the blood (preferentially with the unsaturated fatty acids and particularly with linoleic acid), it seems to be transported more efficiently, and less of it accumulates in the atheromatous plaques.

If you want to reduce the total fat in the diet by 25 per cent and double the polyunsaturated fats, you must decide which foods you most enjoy eating. You must find some way to eliminate many of the highly saturated fats. I know only two ways of doing this. You may cut out whole milk products and butter, or you may cut down a little on meat and modestly on whole milk and eliminate butter completely. As I have pointed out, the most potent source of saturated fat in our diet is milk fat. Incidentally, it would be readily possible to change the fat in milk and thus make milk an important contributor of polyunsaturated fat. This, of course, is not legal, but laws

can be changed! Cutting down on meat fats means consuming leaner cuts of meat. When I speak of meat fats, I mean primarily beef, lamb and pork fats. Poultry and fish contain less fat, and the fat which they do contain has a fair amount of polyunsaturated acids.

The amount of polyunsaturated fatty acids in the diet may be increased by increasing the consumption of (1) the common salad oils (corn, cottonseed and soybean oil), as these run somewhere in the range of 50 per cent linoleic acid, and (2) lightly hydrogenated margarines and shortenings.

It may seem strange that I mention increasing the consumption of certain margarines and shortenings. Many people believe that hydrogenated fats are bad for them, but this is a gullible attitude which stems from believing too much of the current advertising. Actually, most margarines and shortenings are made from soybean oil or, occasionally, from corn or cottonseed oil, and these all contain approximately 50 per cent linoleic acid. It is true that hydrogenation does decrease the amount of linoleic acid, but how much this is decreased depends on how much the oil is hydrogenated. Hydrogenation is a beneficial process that retards rancidity and makes possible the conversion of oils into semisolid form. Moreover, it is a controllable process.

Actually, most margarines and shortenings today contain somewhere between 10 and 15 per cent polyunsaturated acids, and manufacturers of these products are bringing out new ones containing 20 to 30 per cent polyunsaturated acids. This increase in polyunsaturated acids is accomplished by less hydrogenation. It is true that the amount of polyunsaturated acids in these products is a little less than half the amount contained in the original oil, but, in the quantities in which they are used, these products contribute appreciably to the intake of linoleic acid. There are now on the market a number of cooking oils, referred to as "lightly hydrogenated oils," which contain in the range of from 30 to 40 per cent polyunsaturated acids.

In terms of a typical daily menu containing a total of 2600 calories, with 30 per cent coming from fats and with the amount of polyunsaturated fatty acids doubled, one can have a perfectly adequate breakfast which includes fruit and cereal, with skim milk on the cereal. (Many people do not like the taste of skim milk, but sooner or later the dairies will realize that if they simply increase the amount of milk solids they can have milk which tastes, looks and "feels" like whole milk and which really is an excellent product.) The breakfast menu also may include an egg, two pieces of toast, and coffee with sugar. The only real difference between such a breakfast and the one that many of us have is, perhaps, that it includes one egg rather than two eggs. Another difference may be that there is, of course, no bacon, ham or sausage accompanying the egg.

Lunch on this typical menu may include soup, a chicken sandwich, fruit and coffee, tea or skim milk.

For dinner, as for breakfast and lunch, I have tried to make recommendations which are more or less realistic for the majority of individuals. Many people like to have a cocktail or two before dinner; that is perfectly all right as long as they realize that there are 7 calories per gram in the alcohol. In considering the meal itself, 3 oz. of beef is sufficient. The size of the steak which a number of restaurants serve exceeds considerably that limitation; however, 3 oz. of beef is about what one gets for dinner on a plane, and I have yet to find anyone who, if the food served on a plane has been well prepared, is hungry after eating it.

The quantity of food consumption is in part a matter of habit. The evening meal may include meat, potatoes, vegetable, salad, pie (if one wishes it) and coffee. A bottle of beer or a highball and some pretzels in the evening are perfectly all right as long as the caloric content is considered. I think that probably the most important thing to remember concerning the menu suggestions is the total figure of 2600 calories per day. This caloric content requires smaller servings than most of us are accustomed to, particularly if it is to include a cocktail or a bottle of beer.

These dietary suggestions can be summarized very briefly. I think it is probably desirable and in accord with the experimental as

well as the epidemiologic pattern of reducing the chances of development of coronary disease to reduce, at least moderately, our intake of calories coming from fat. In general terms, this means a moderate decrease in meat fats, a drastic decrease in whole milk and milk products containing fat, a decrease in (but not elimination of) eggs, and a decrease in the amount of table spread used. It means an increase in cereal, fish and poultry, skim milk and pastries made with cottonseed, soybean or corn oil or margarines or shortenings prepared so that they contribute effectively to our intake of polyunsaturated fats.

Factors in Coronary Artery Disease

The following factors are known to affect or to be associated with coronary artery disease in man: heredity, overweight, elevated serum cholesterol, increased diastolic blood pressure, cigarette smoking and exercise. The physician can do something about the last five, including even physical activity. The patient also can pay heed to these five factors and act accordingly if he is sufficiently motivated to do so.

I believe that the single most important thing for us to realize about these various factors is that they are additive. For example, if a patient has a strong family history of cardiovascular disease, is overweight, has an elevation of serum cholesterol, has had a slight increase in diastolic pressure, is a heavy cigarette smoker, and has sedentary habits, he is an especially likely candidate for development of coronary artery disease at an early age.

On the other hand, if a patient's parents lived into their seventies or eighties, if he is of average weight, if his blood pressure is normal, if he is not a heavy smoker, and if he is moderately active, a slightly elevated level of serum cholesterol probably is not too important.

In a practical sense, the role of nutrition today in cardiovascular disease is limited to its effect on body weight (i.e., total caloric intake), the over-all effect of a well-balanced diet, and its effect on the level of serum cholesterol. Thus, nothing is to be gained by trying to manipulate the diet of adults who have serum cholesterol levels that are in the range of 200 mg. per cent, are of desirable body weight, and consume a varied diet of meat, fish, milk products, eggs, cereals, fruits and vegetables.

ACKNOWLEDGMENT

The research done for this paper at the Department of Nutrition, Harvard University School of Public Health, Boston, was supported by a series of grants from The John A. Hartford Memorial Fund; National Institutes of Health; Nutrition Foundation, Inc., Albert and Mary Lasker Foundation, Inc., and the Fund for Research and Teaching, Department of Nutrition, Harvard University School of Public Health.

Appraisal of Needle Biopsy

RAYMOND BANGLE, JR.*

Cancer Detection Clinic, Los Angeles

If properly performed, needle biopsy is a useful diagnostic procedure which often is more advantageous than other biopsy methods. It is safe, expeditious and inexpensive. Needle biopsy consists of (1) aspiration of bits of tissue or of a core of tissue through the needle into the syringe or (2) cutting of a core of tissue which is withdrawn with the biopsy needle.

The author describes the means by which an adequate specimen can be procured, the contraindications and potential complications of needle biopsy, and the known problems relating to the use of this procedure at specific anatomic sites.

NEEDLE biopsy has been practiced from time to time for about a century. In 1926 it became almost routine diagnostic procedure at the Memorial Center for Cancer and Allied Diseases, New York.[1,2] Its frequent use at this and other medical institutions has proved that needle biopsy is safe, relatively simple, timesaving, reliable and usually inexpensive.[3-5] It is surprising that even with the development of improved needles and technics for biopsy, this method still has not achieved widespread popularity. The purpose of this article is to review and appraise the use of needle biopsy as a definitive diagnostic procedure in the physician's office, clinic or hospital.

RAYMOND BANGLE, JR.

Incisional, excisional and needle biopsies are the principal types of biopsy currently in use. The various kinds of needle biopsy are outlined in table 1.

Requirements

As with any type of biopsy, the successful use of needle biopsy depends on the following:

1. Cooperation between the clinician and pathologist.
2. Knowledge of indications, limitations

*Director of Laboratories and Research, Cancer Detection Clinic, Los Angeles, California.

TABLE 1

TYPES OF NEEDLE BIOPSY

TYPE	BASIC EQUIPMENT	BASIC PROCEDURE
Aspiration of core of tissue	Record syringe (20 cc.); approximately 14 gauge needles of different lengths with obturators or biopsy needle such as the Franseen type	Aspirate intact core of tissue into syringe containing normal saline; transfer to fixative; process for paraffin sections
Aspiration of bits of tissue	Syringe appropriate for securing high negative pressure (20 cc.); 18 gauge needles of varied lengths with obturators; a metal or wood instrument to rake specimen from barrel of syringe	Pull out plunger of syringe; gently move needle within the tumor; release negative pressure after obtaining material in syringe; use rake to remove material from syringe; preparation of smears or sections, or both
Nonaspiration; direct removal of core of tissue	The Vim-Silverman biopsy needle or Franklin modification, the Turkel biopsy needle, or the Hutchins biopsy needle	*In situ* detachment of core of tissue removed together with the biopsy needle; transfer tissue to fixative; process for paraffin sections

and potential complications of the procedure.

3. Careful technic, skill and judgment of the clinician.

4. Careful histologic technic and adequate diagnostic experience of the pathologist.

The failure to obtain an adequate and representative specimen by needle biopsy may be due to technical or operative difficulties. The failure to obtain satisfactory histologic sections of a needle biopsy specimen may result from poor histologic technic, including improper preservation of the specimen. Only by close cooperation between clinician and pathologist can needle biopsy serve as a useful diagnostic procedure and in many instances prove more advantageous than other types of biopsy.

Biopsy should never be regarded as a shortcut diagnostic procedure. Each case considered for biopsy demands a thorough and careful evaluation of the clinical history, physical examination, relevant radiologic findings and pertinent hematologic and other laboratory data. Only then can it be decided which particular type of biopsy procedure will yield the greatest diagnostic accuracy with the least potential danger to the patient.

Indications

The basis of good medicine is a precise diagnosis of the patient's disease. We now are in an era of increasing use of needle biopsy as a definitive diagnostic procedure which in certain instances is also of prognostic value. Largely through the development of improved biopsy needles and technics, its use has broadened.

General indications for needle biopsy include the following:

1. A palpable lesion deep in soft tissue and covered by normal tissue, such as a localized lesion of the breast.

2. Conditions suspected clinically to be diagnosable only on biopsy, as certain lesions of the bone marrow, liver, spleen, kidneys, pleura, prostate gland, brain and pancreas.

3. Clinically apparent, deep-seated lesions suspected of involving or found at exploratory operation to involve an anatomic structure wherein surgical incisional or excisional biopsy is likely to be difficult, hazardous or unrepresentative.

From the standpoint of the doctor's office or hospital, the practical application of needle biopsy usually is limited to select cases in which the physician is dealing with a diagnostic problem, such as fever of unknown origin, and in which other surgical biopsy procedures are apt to be hazardous or unrepresentative. The decision as to whether needle biopsy is to be performed blindly (closed biopsy) or after surgical exposure of the diseased tissue (open biopsy) depends largely on the clinician's skill and judgment.

FIGURE 1. Instruments used for an aspiration biopsy include a 20 cc. syringe, which is suitable for providing high negative pressure, and an 18 gauge needle or needle of larger caliber if core of tissue is to be aspirated. An obturator for the needle and an instrument for raking aspirated material from the barrel of the syringe also are employed.

Needle biopsy is employed by staff members at the Hospital of the Good Samaritan, Los Angeles, principally in suspected tumors of the prostate gland, brain, pancreas and soft mesenchymal structures and in lesions of the liver, spleen and bone marrow. Its use is sporadic but not rare in lesions of the breast, lymph nodes and kidneys. It is employed rarely in lesions of the salivary glands, thyroid gland, pleura, lungs and bones. Needle biopsies of the brain, pancreas and spleen are performed only under surgical exposure and direct visualization. Aspiration biopsy of the endometrium has been practiced successfully and safely in the physician's office, principally in cases of postmenopausal bleeding or in patients who refuse hospitalization for the conventional diagnostic uterine curettage. Requests for more frequent performance of needle biopsy usually originate from internists dealing with cases of undiagnosed renal pathology, suspected diffuse vascular disorder, and pleural effusion of unknown etiology.

Technics

The ultimate value of biopsy depends on the combined success of the clinician in securing a proper specimen and the pathologist in properly interpreting the histologic findings. Needle biopsy is not popular among those who, because of inadequate technic, either fail to obtain any tissue or do not secure a representative specimen. This problem has been overcome largely by the use of improved biopsy needles. It is advisable to learn the procedure with one biopsy needle suitable for a particular anatomic region. The technic may be practiced on tissue that is to be discarded.

The equipment required for aspiration biopsy is simple, namely, a 20 cc. Record syringe (or syringe in which high negative pressure can be obtained), 18 gauge needles of different lengths with obturators, and a metal or wood instrument designed as a rake for removing the aspirated specimen from the barrel of the syringe (figure 1).

In certain instances the principle of aspiration biopsy may be adapted to dislodge a core of tissue. This has been of particular value in biopsy of organs such as the liver and spleen. A smaller gauge needle to which a syringe can be attached securely is necessary. The Franseen biopsy needle is particularly useful, since it has a cannula with a sharp, serrate end instead of a beveled one and an obturator with a conic tip (stiletto). To prevent splattering of the aspirated core of tissue in the syringe, the latter is partly filled with normal saline (figure 1).

Of a number of commercially available biopsy needles, the Vim-Silverman needle (figure 2a) probably has been the most popular. It consists of an outer needle or cannula with a beveled end and stylet obturator for insertion into the tissue. In addition, there is an inner cutting device which replaces the obturator and is inserted into the lesion to obtain a core of tissue. However, removal of

FIGURE 2. a. The Vim-Silverman biopsy needle, comprised of (from left to right) an outer needle with a smooth handle and beveled end; an obturator with a beveled end; and an inner, partly split cutting device.

b. The Hutchins biopsy needle, which has (from left to right) an outer needle with corrugated handle and a sharp, serrate end; an obturator with a conic tip; and an inner cutting device with metal bars filling the convexity of each blade only at the tip.

the required core of tissue is not always accomplished. To assure removal of a core of tissue during withdrawal of the biopsy needle, a simple modification of the inner cutting device has been made. This consists of a small bar of metal at the tip of the cutting device, as shown in figure 2b (the Hutchins biopsy needle). When taking a biopsy with the Hutchins needle or a similar instrument, the outer needle is advanced over the inner cutting component. This causes approximation of the metal bars at the tip of the split component of the cutting device, with resultant detachment and retainment of the core of tissue. The latter then is removed together with the biopsy needle. When applied to the Vim-Silverman biopsy needle, this is known as the Franklin modification.

The newer biopsy needles, particularly the Hutchins type, incorporate other desirable features (figure 2b). These consist of an outer needle and cutting device of slightly larger caliber, an outer needle with a sharp, serrate cutting end, and an obturator with a conic tip (stiletto), providing greater control and ease during insertion of the needle. Further, the Hutchins biopsy needle has a corrugated handle of appropriate size and configuration to facilitate manipulation.

Necessarily, the biopsy procedure will depend to a variable extent on the anatomic site to be biopsied, the biopsy needle and equipment employed, and the skill acquired through experience. Aseptic technic must be used in handling the specimen if bacteriologic studies are to be done.

Prevention of Artefacts

The needle biopsy specimens necessarily are small and easily distorted by mechanical pressure, heat, drying and improper fixation. It is imperative that the specimen be obtained, handled and preserved under the most favorable conditions.

Histologic artefacts may be prevented through the cooperative efforts of the surgeon, pathologist and tissue technician. The more frequent causes of distortion of the tissue obtained by needle biopsy are presented in table 2.

Insofar as the adequacy of histologic preparations is concerned, the primary responsibilities of the clinician performing such biopsy include the following.

TABLE 2

ARTEFACTS AND THEIR PREVENTION IN THE USE OF NEEDLE BIOPSY

EFFECT	CAUSE	PREVENTION
Mechanical compression on the core of tissue	1. Use of biopsy needle with inner cutting device of insufficient caliber 2. Use of biopsy needle with inner auger-type device 3. Use of forceps in removing specimen from inner device 4. Use of forceps in any phase of handling the specimen	1 and 2. Use appropriate biopsy needle, such as the Hutchins type 3 and 4. Use a toothpick or similar object for removing and handling the specimen or use normal saline for washing specimen from inner device
Mechanical splattering of the aspirated specimen	Use of prolonged or excessively high negative pressure, or both, in the syringe for securing the aspirated specimen; compressing specimen in removing it from the barrel of the syringe	After material is obtained in the syringe, release the negative pressure promptly; use metal instrument to rake the aspirated material from the barrel of the syringe
Cells obscured or partly lost in making smears and sections	1. Excess amount of blood or allowing the blood to clot 2. Improper preparation of smears	1. Promptly release negative pressure in syringe when aspirated material is obtained; if tissue is unusually bloody, rapidly transfer it to fixative containing heparin or citrate 2. Avoid use of adsorbent material (cotton) in removing aspirated material from syringe and in making smears
Inadequate cellular details	1. Improper preservation (fixation) of the specimen 2. Inadequate histologic technic	1. Except for air-dried smears, the specimen should be placed rapidly into an appropriate fixative for a period to insure complete chemical fixation

1. Use of appropriate biopsy needle.

2. Prompt but gentle transfer of the specimen into an appropriate fixative. The specimen may be handled adequately by use of a toothpick, as illustrated in figure 3.

3. Prompt preparation of smears, avoiding the use of cotton for handling or smearing the aspirated material.

Properly prepared smears which are air-dried rapidly may be stained immediately and satisfactorily by the conventional hematoxylin-eosin method. If the Papanicolaou staining method is to be used, the smears should be placed quickly into an appropriate fixative. The Papanicolaou method, in comparison with the air-dried hematoxylin-eosin method, is time-consuming, costly, subject to more pitfalls, and not uncommonly less diagnostic since usually fewer smears are processed.

If the biopsy specimen consists of cores of tissue, the entire specimen should be processed for multiple histologic sections representing different levels in cutting through the thickness of the tissue. The only exception to this is when bacteriologic studies are to be done on a part of the specimen.

Advantages of Needle Biopsy

Needle biopsy when indicated and used properly is safe, expeditious, relatively simple, reliable and usually inexpensive. In many instances it may be performed without untoward events in the clinic or physician's office. Its reliability as a precise diagnostic procedure not uncommonly exceeds that of surgical incisional biopsy of a superficial "wedge" type. This is exemplified, as shown in figure 4, by the following situations: (1) In lesions of the liver and pancreas, needle biopsy under direct visualization enables more adequate and representative sampling since it can be performed easily at different levels and depths with correspondingly increased diagnostic accuracy, while superficial "wedge" biopsies may be nondiagnostic or, because of capsular or subcapsular fibrosis, misdiagnosed. (2) In pros-

tatic lesions and tumors surrounded by a fibrous capsule, needle biopsies at different depths are more likely to be diagnostic than is a superficial incisional biopsy which may consist only of connective tissue.

Surgical excisional biopsy is the procedure of choice in certain instances. At other times it is undesirable, particularly in conditions in which its performance might be difficult or hazardous. There also are cases in which any form of biopsy may seem equally satisfactory, as in a localized breast lesion. However, if a breast lesion is clinically suggestive of cancer, the size, location and degree of mobility of such lesion on palpation are factors to be considered in deciding on a particular biopsy procedure. For example, if the tumor is very small and movable, it may be difficult or impossible to steady the lesion adequately with one hand while inserting the biopsy needle. In such a situation excisional biopsy is preferred. In larger tumors of the breast, aspiration biopsy through an 18 gauge needle certainly is desirable in that it is simpler and less traumatic than other types of biopsy. However, the value of this procedure depends on the diagnostic experience of the pathologist.

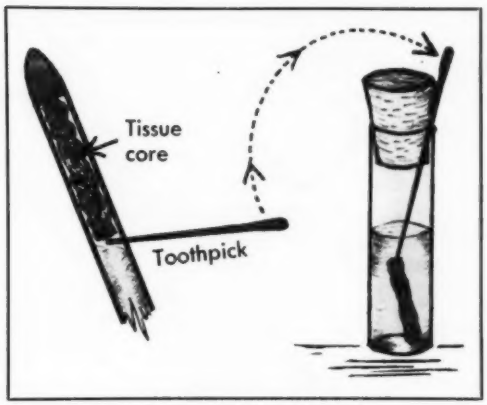


FIGURE 3. Use of toothpick in handling and transferring core of tissue from cutting device of the Hutchins-type biopsy needle to appropriate fixative.

Contraindications and Complications

General aspects—Each case considered for biopsy requires keen judgment and evaluation as to the particular type of biopsy procedure most likely to yield an exact diagnosis with the least potential harm to the patient. The advantage of needle biopsy is that it procures tissue in a relatively simple way. In doing needle biopsies there are certain contraindications which may seem obvious; others may seem less obvious, and still others may be debatable. For general consideration, these include infections occurring in the needle tract, hemorrhage and hemorrhagic disorders, implantation of cancer along the needle tract, and metastatic dissemination of cancer through lymphatics and blood vessels.

Infections occurring in the needle tract—A potential or theoretical complication of needle biopsy is the spread of an infectious process along the needle tract. Undoubtedly, this may result. However, in many large series of cases wherein needle biopsy was indicated and performed by clinicians experienced in the procedure, the dissemination of infection in the

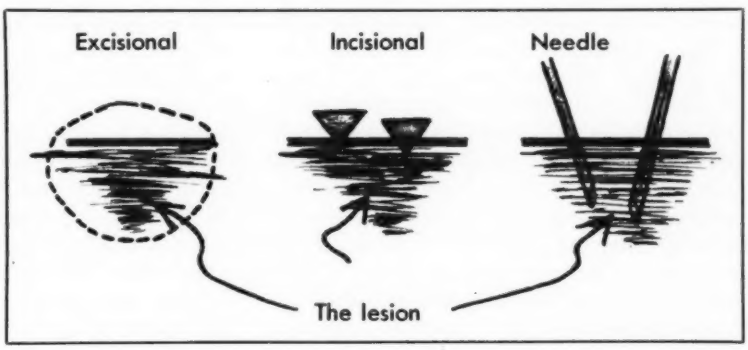


FIGURE 4. Diagrams of excisional, incisional and needle biopsies of a lesion (e.g., situated beneath capsule of liver, or encapsulated tumors), illustrating why needle biopsy easily provides more adequate specimens in comparison with those obtained by superficial incisional biopsies.

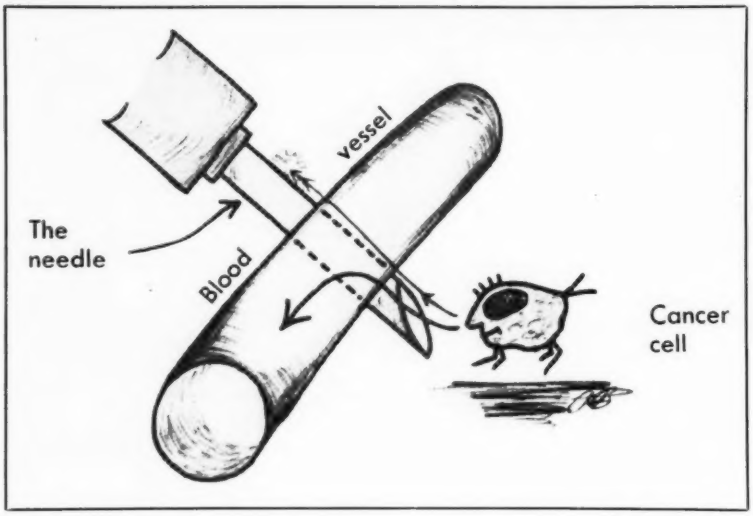


FIGURE 5. Diagram of two potential complications of needle biopsy, namely, entrance of cancer cells into a blood vessel punctured by the needle and spread of cancer cells along the needle tract.

needle tract either did not result or occurred rarely. This includes a large series of prostatic,[6] renal, pleural and sternal bone-marrow[4] biopsies, totaling 932, 800, 1,155 and 5000 cases, respectively. In this series there was not one instance of resultant draining sinus tract or dissemination of the subsequently proved infection, including tuberculosis.

Hemorrhage and hemorrhagic disorders—A biopsy needle should not be inserted blindly into a lesion situated in close proximity to vital structures which, if damaged, might lead to a serious complication. That large blood vessels, myocardium and viscera have been punctured without any serious consequences does not justify the indiscriminate use of the procedure.

In individuals with a hemorrhagic disorder, needle biopsy is contraindicated unless there is some means of preventing or controlling the abnormal bleeding state. In screening the patient for the possible existence of a hemorrhagic disorder, laboratory tests should never be substituted for eliciting a detailed history from the patient in an attempt to learn of any incident which might suggest an abnormal bleeding tendency. One should search carefully under optimal lighting conditions for petechiae and ecchymoses, particularly at the site of venipuncture or hypodermic injection.

Dissemination of cancer—A great deal of fantasy, fallacy and fiction has clouded the facts and evoked fear in regard to two potential or theoretical complications of needle biopsy, namely, implantation of cancer along the needle tract and metastatic dissemination of cancer through lymphatics and blood vessels (figure 5).

Although there is no doubt that spread of cancer along the needle tract may occur, there also is no doubt that in the innumerable instances wherein the needle tract remains this occurrence is so rare that documented case material is almost nil.[3,4,6,7] Furthermore, in many instances in which the lesion proved to be malignant on needle biopsy, the subsequent definitive surgery resulted in continuous excision of the tract with the remainder of the specimen, thus obviating this theoretical danger. Although definitive surgery is performed usually one or a few days after the needle biopsy procedure, the exact interval in delay does not seem to be a critical factor. Thus, needle biopsy of a subsequently proved mammary carcinoma may be performed safely in the doctor's office, following which the patient may be scheduled for hospitalization. If results of the biopsy are reported negative for cancer, although the lesion remains clinically suggestive of tumor, the patient should be

scheduled for open surgical biopsy. In several thousand cases, regardless of the period of delay in days, histologic studies have failed to reveal cancer elements in the needle tract of the subsequent radical mastectomy specimen.[6] Other studies in which an attempt was made to recover cancer cells from the needle tract by tissue culture technics occasionally have been successful.

That needle biopsy may eventuate in dissemination of cancer cells through lymphatics and blood vessels is true. However, the objection to needle biopsy on this basis is theoretical. Furthermore, the same objection may be made to other forms of biopsy, to trauma, to palpation of a tumor, and to surgical manipulation of a tumor. It is true that as a result of any of the above mechanical effects, the condition may become optimal for the entrance and circulation of cancer cells in lymphatics and blood vessels. It likewise is true that even though this process occurs spontaneously and commonly in many individuals with cancer it is of no known prognostic value.[8-10] Only by recently developed laboratory technics has it been possible to isolate cancer cells from blood with greater reliability and accuracy.[8-10]

Specific anatomic sites—Liver and spleen—Needle biopsies of the liver and spleen, especially if performed blindly, are potentially hazardous. According to the frequency with which he performs them, the physician becomes either overcautious (and cuts down on the number of them) or overenthusiastic (and gets into trouble sooner or later). Hemorrhage is a serious complication subsequent to puncture of a vascular hepatic cancer or hemangioma. It is impossible to predetermine the existence and location of an unusually vascular lesion or the possible occurrence of abnormal bleeding after puncture of such lesion. It is reasonable, certainly safer, and usually more reliable to perform needle biopsies of the liver and spleen selectively and at various levels only after open surgical exposure of these organs. If an unusual degree of bleeding follows withdrawal of the needle, even from a large cavernous hemangioma of the liver, it then may be possible to control this by direct insertion of GELFOAM® into the needle tract.

A serious complication of liver biopsy in cases of obstructive jaundice is uncontrolled bile peritonitis subsequent to withdrawal of the biopsy needle from the liver or unintentionally punctured gallbladder.

Kidneys—Renal biopsy should not be performed in a patient who has only one kidney, in the uremic patient with oliguria and progressively rising blood nonprotein nitrogen, or in an uncooperative patient who fails to follow the given instruction of holding his breath at the height of inspiration, at which time the biopsy specimen is taken. In a series of 800 renal biopsies,[4] a mild transitory microscopic hematuria frequently occurred, but the incidence of self-limited gross hematuria was only 6 per cent; that of recurrent hematuria was 2 per cent. The recurrent hematuria also was self-limited after a longer period of bed rest. Only in two cases did a perirenal hematoma develop.

Pleura—Except in cases of a tendency toward abnormal bleeding, there are no specific contraindications for pleural biopsies. Actual complications comprise small pneumothorax and mild hemoptysis if the lung is punctured unintentionally, but these usually are not serious and can be treated. In a large series of needle biopsies of the parietal pleura, the theoretical complications of air embolism and of draining sinus tract, such as in subsequently proved tuberculous pleuritis, have not been observed.[3,4]

Thyroid gland—The use of needle biopsy in thyroid lesions is somewhat debatable. Problems likely to arise sooner or later on performing blind biopsies of the thyroid include (1) difficulty in immobilization of the thyroid gland, with corresponding difficulty in obtaining a representative specimen; (2) possible occurrence of hemorrhage in the thyroid gland or the neck; (3) difficulty in or impossibility of differentiating microscopically between the diagnoses of follicular adenoma, follicular carcinoma and nodular adenomatous goiter; and (4) possible failure by needle biopsy to uncover a cancer coexisting with diffuse thyroiditis. Whenever possible, surgical exposure of the thyroid gland is ad-

visable. At this time, if so indicated, an appropriate biopsy procedure including needle biopsy may be performed.

Lymph nodes—In a patient with lymphadenopathy, localized or generalized and suspected clinically to represent lymphoma, metastatic tumor or inflammatory process, a surgical excisional biopsy of one or more enlarged nodes usually is the procedure of choice. The more focal a disease process in an enlarged lymph node the more likely it is that it will be missed by needle biopsy. Furthermore, in a case of lymphoma, a definitive diagnosis often depends on careful histologic study of the entire lymph node. However, if there is a clinically suspicious metastatic tumor involving one or more cervical lymph nodes, needle biopsy is desirable in order to facilitate subsequent surgery if radical dissection of the neck is to be performed.

Sternal bone marrow—Except in cases of a tendency toward abnormal bleeding, there are no specific contraindications for needle biopsy of the sternum. Rarely, retrosternal hematoma may result.[4] The primary objective of the bone-marrow biopsy is to obtain marrow in a state simulating that *in situ* and not altered by admixture with peripheral blood. This requires removal of an intact core of marrow through the needle, adequate fixation of the specimen (preferably in Zenker's fixing fluid), and properly stained sections. Only then is it possible to observe and identify cells in an undisturbed histologic setting. Examination of stained smears of bone marrow is less reliable in many instances for making a precise diagnosis.

REFERENCES

1. Martin, H. E. and Ellis, E. B.: Biopsy by needle puncture and aspiration. Ann. Surg. 62:169-181, 1930.
2. Stewart, F. W.: The diagnosis of tumors by aspiration. Am. J. Path. 9:801-812, 1933.
3. Godwin, J. T.: Aspiration biopsy. J.M.A. Georgia 46:537-542, 1957.
4. Hussey, H. H.: The needle biopsy—when and why? (Panel discussion.) Audio-digest, Internal Medicine (September 21) 1959, vol. 6.
5. Smetana, H. F.: The needle biopsy in diagnosis. Am. J. Clin. Path. 24:395-405, 1954.
6. Bangle, R., Jr.: Unpublished data.
7. Ackerman, L. V. and Wheat, M. W.: The implantation of cancer—an avoidable surgical risk? Surgery 37:341-355, 1955.
8. editorial: Malignant cells in the blood stream. Brit. M. J. 1:774-775 (March 21) 1959.
9. Engell, H. C.: Cancer cells in the blood. Ann. Surg. 149:457-461 (April) 1959.
10. Sandberg, A. A., Moore, G. E., Crosswhite, L. H. and Schubarg, J. R.: The frequency of tumor cells in the bone marrow and blood. Cancer 11:1180-1186, 1958.

MEETINGS *and Postgraduate Courses*

American College of Surgeons, Winnipeg, Manitoba: Sectional meeting to be held at the Fort Garry Hotel, April 6-8. For further information, write to: Dr. Robert S. Myers, Public Relations Department, American College of Surgeons, 40 East Erie Street, Chicago 11.

American Orthopsychiatric Association, New York: Thirty-eighth annual meeting, March 22-25, at the Hotel Statler-Hilton. For further information, write to: Dr. Marion F. Langer, Executive Secretary, American Orthopsychiatric Association, 1790 Broadway, New York 19. Registration open to nonmembers as well as members.

Emory University School of Medicine, Atlanta: Postgraduate course on physical examination of the cardiovascular system, March 10-11, at the Grady Memorial Hospital Auditorium. For further information, write to: Department of Medicine, Emory University School of Medicine, 69 Butler Street S. E., Atlanta 3.

International Federation of Gynaecology and Obstetrics, Vienna, Austria: Third world congress to be held September 3-9, 1961. For further information, write to: Doz. Dr. V. Grünberger, Scientific Secretary, Medizinische Akademie, Alserstr. 4, Vienna 9, Austria.

Uterine Bleeding in the Second Trimester Caused by Abnormal Placental Development

J. EDWARD HALL*

State University of New York Downstate Medical Center, Brooklyn

Uterine bleeding in the second trimester may result from abnormalities that are not specific to this period of gestation, but certain abnormal placental developments are more prone to produce symptoms between the twelfth and twenty-eighth weeks than at other times. The three such conditions discussed are circumvallate placenta, hydatidiform mole and choriocarcinoma.

Circumvallate Placenta

CIRCUMVALLATE placenta has not received the attention it warrants, and the literature contains few articles about it. While complete circumvallate placenta occurs only about once in every 160 pregnancies, partial degrees of this abnormality are far more common than is generally recognized. It has an incidence not dissimilar to that of placenta previa. It is found more frequently in multiparas than in primiparas. Williams' explanation of the etiologic basis for the entity is the one most commonly accepted. However, why the chorion frondosum is small, leading to the later extension of the chorionic villi, is not clear.

If symptoms develop, they appear at about the twentieth week, which is earlier than the appearance of symptoms in most cases of placenta previa. There are three symptoms associated with circumvallate placenta: vaginal bleeding, hydrorrhea and intermittent uterine contractions. Vaginal bleeding occurs in about 50 per cent of the cases, hydrorrhea in 25 per cent, and intermittent uterine contractions in 20 per cent. If these symptoms appear during the second trimester, the possibility of a circumvallate placenta should be considered.

In most cases in which bleeding occurs, the amount of blood lost is not large and the patient can be treated expectantly after one has ruled out local lesions as the cause of bleeding by examination of the vagina and cervix with a speculum. However, if bleeding

*Departments of Obstetrics and Gynecology, State University of New York Downstate Medical Center and Kings County Hospital Center, Brooklyn, New York.

continues and a large amount of blood is lost, a double-setup vaginal examination, as would be done in suspected placenta previa, should be performed.

Thirty per cent of the cases of nontoxic separation of the placenta are associated with complete or partial circumvallate placenta. This is caused by degenerative changes in the decidua overlying the extrachorionic portion of the placenta. This area is particularly vulnerable to disruption by minor trauma or even slight uterine contractions because it is no longer protected by the heavy resistant chorionic plate. As a result of this premature separation there is a very high rate of prematurity associated with circumvallate placenta, in some reports as high as 45 per cent. The fetus may be in jeopardy not only because of prematurity but also because of placental insufficiency which may lead to intrauterine death.

The two most important entities to consider in the differential diagnosis are placenta previa and premature separation of a normally implanted placenta.

The conduct of labor and delivery is normal in most cases. However, there may be some difficulty in the third stage, leading to abnormal bleeding. The placenta may separate improperly, and the membranes may shear off from the placenta. It is therefore important to examine the placenta carefully to be certain it is intact and the membranes are present.

Hydatidiform Mole

This abnormality of placental development affects the chorionic villi. The villi increase in number, become hydropic and avascular, and show proliferation of the trophoblast. Various figures on the incidence of hydatidiform mole are given in the literature, but an accepted rate of occurrence in this country is once per 2000 pregnancies. The majority of the patients are between 25 and 35 years of age, but women over 40 years old show a relatively high incidence of these pathologic products of gestation.

The most consistent symptom of hydatidiform mole is vaginal bleeding, small to moderate in amount and appearing first in the second trimester. Although textbooks emphasize the presence of a uterus larger than normal for the period of gestation, in some series of cases of hydatidiform mole such an enlarged uterus has been present in less than 50 per cent. Absence of fetal movements and fetal heartbeat associated with enlargement of the uterus to a size larger than a five month gestation should arouse suspicion of the presence of a hydatidiform mole.

Symptoms of toxemia prior to the twenty-fourth week of gestation may contribute to the diagnosis. Patients with symptoms of severe toxemia associated with a hydatidiform mole have an unduly enlarged uterus or a pregnancy of more than 16 weeks' duration.

Enlarged ovaries due to corpus luteum cysts are found in less than 50 per cent of all cases and in some series have been present in less than 10 per cent. When present, they may be of considerable size and are an aid in the follow-up of the patients.

Hormone production—Chorionic gonadotropin is produced by the trophoblast, most likely the cytotrophoblast, and since hydatidiform mole is associated with an increased amount of trophoblast, usually there is an increased amount of chorionic gonadotropin. A single determination of chorionic gonadotropin has little value, but repeated determinations showing an increasing production between the tenth and the twentieth week of gestation are very suggestive of the presence of a hydatidiform mole. However, it is difficult to establish a level above which one can definitely state that a mole is present. It would appear that a titer of 500,000 I.U. or more per liter of urine usually is indicative of a hydatidiform mole. If the biologic test is used, the Aschheim-Zondek method is the most reliable.

While chorionic gonadotropin may be excreted for several weeks after removal of a hydatidiform mole, 80 per cent of the patients will have no demonstrable hormone one month following its removal. Presence of chorionic gonadotropin after this period of time suggests the presence of malignant trophoblastic epithelium. Nevertheless, a persistent decline in amount is more significant than the mere presence of the hormone.

Determination of chorionic gonadotropin in the blood serum is more accurate than measurement of its level in the urine; most workers have abandoned testing of the cerebrospinal fluid because of the unreliability of results.

The pathologic diagnosis of hydatidiform mole is established by the presence of dilated hydropic chorionic villi that are also avascular and have proliferation of the trophoblastic epithelium. Since the possible subsequent development of malignant features is a prime consideration, several efforts have been made to establish histologic criteria to aid in diagnosis. Hertig and Sheldon[1] in 1947 divided their series of hydatidiform moles into six categories based on degree of hyperplasia and anaplasia of the trophoblast. This classification is quite complex and has not found general acceptance. However, it is true that a marked but not absolute correlation exists between the degree of trophoblastic proliferation and anaplasia and the tendency for the development of a malignant process.

Hunt, Dockerty and Randall[2] in 1953, using another method of grading, concluded that a careful observation of the clinical course after removal of a hydatidiform mole was more important than mere histologic examination.

Treatment—It should be obvious that it is not always easy to be certain of the diagnosis of hydatidiform mole. The most certain evidence is the passage of chorionic vesicles. However, once the diagnosis is established the uterus should be emptied. If the uterus is smaller than the size of a 16 week gestation, medical induction with an infusion of oxytocin followed by a thorough curettage may be done. If the uterus is larger, abdominal hysterotomy is preferable. The uterine cavity should be curetted at the time of the hysterotomy, following removal of the mole.

The patient should be seen every four weeks for the first six months after removal of the mole. Follow-up investigation should include an adequate history, physical examination and determinations of chorionic gonadotropin. If uterine bleeding continues, curettage should be performed. Persistence of chorionic gonadotropin with little or no decrease in amount at the end of 60 days is indicative of the presence of functioning trophoblast. In such a case, one should seriously consider hysterectomy at this time even if there are no abnormal physical findings and curettage has demonstrated normal epithelium, since invasion of the myometrium may have occurred. The ovaries can be preserved to continue their production of estrogen.

Choriocarcinoma

Choriocarcinoma is a malignant development of the trophoblastic epithelium. Many terms have been applied to this tumor, but choriocarcinoma is the one most widely used today and is accurately descriptive.

Disturbances in the regulatory mechanism of trophoblastic activity may play an important role in the development of choriocarcinoma. The tumor consists of tissue with peculiar features and differing from all other human tissues by its own physiologically determined duration of life (38 weeks). Probably the malignant properties of the tumor are influenced unfavorably by this hereditarily determined short lifetime and by its great dependence on maternal blood supply. The complete absence of any adequate blood supply, which in each instance results in extensive necrosis, increases the vulnerability of the very active cells.

The degree of malignancy may depend on the age at which the trophoblastic cells become detached from the ovum and begin their autonomous existence. The earlier this occurs, the less differentiated they are and the greater is their malignant potential.

A satisfactory explanation has not been given for the periods of inactivity of potentially malignant chorionic elements. Investigation is necessary to determine the stimulus that reactivates dormant trophoblastic cells.

Choriocarcinoma is a rare tumor, occurring about once in every 10,000 pregnancies in the United States. It may follow any type of gestation, normal as well as pathologic. The highest incidence of choriocarcinoma is found in women who have had hydatidiform mole. About 2 to 3 per cent of these moles become choriocarcinomas, and these cases account for 50 per cent of all choriocarcinomas. The tumor may occur at any age after the menarche. The

youngest patient described in the literature was 14 and the oldest was 79 years of age.

Symptoms associated with choriocarcinoma vary widely. There is no standard pattern. The most frequent symptoms are nausea, vomiting, abdominal pain, dysuria, cough, hemoptysis and vaginal bleeding. Cerebral symptoms may be present if the brain is involved.

Chorionic gonadotropin is almost always present, and usually in large amounts. The amount should be determined in actual units, but the biologic dilution test using the Aschheim-Zondek method may be employed.

Diagnosis of choriocarcinoma by histologic examination of any removed tissue has been considered final, but in some cases, especially in the early phases, there may be divergent opinions. Moreover, the tumor may exhibit varying patterns in the same patient, and therefore many areas should be examined. The histologic diagnosis is based on finding anaplastic trophoblastic epithelium, usually both cytotrophoblast and syncytiotrophoblast, associated with hemorrhage and necrosis. The finding of definite villi poses a problem of classification. Some authorities have stated that the presence of villi rules out the diagnosis of choriocarcinoma. However, in recent years authentic cases of choriocarcinoma have been accepted in spite of the presence of chorionic villi. Nevertheless one should be cautious in making the diagnosis of choriocarcinoma when villi are seen.

The diagnosis of choriocarcinoma from uterine curettings is often most difficult even in expert hands. Frequently, presence of the tumor is suspected and the patient is treated in the absence of tissue examination, on the basis of clinical aspects of the case, including high levels of chorionic gonadotropin. Although such a procedure is undesirable, one is obligated to carry it out rather than run the risk of not removing malignant trophoblast. A roentgenogram of the lungs should be included in the study of any suspected case, as they are a frequent site for metastases.

Once the diagnosis of choriocarcinoma is made, active therapy is indicated. Involved tissue that can be removed surgically with safety should be removed. Thus a complete abdominal hysterectomy should be performed in most cases. If the ovaries are normal, they should be preserved to continue the production of estrogen. Results of x-ray therapy are equivocal and it is not employed as much today as it was a few years ago.

Chemotherapy has offered a new hope in the treatment of choriocarcinoma. The agent employed most frequently is methotrexate, a folic-acid antagonist which may have toxic side effects. Hertz[3] has been one of the main advocates of its use. Some miraculous arrests of the malignant process and possibly some cures have resulted from the use of this drug. Much more experience with methotrexate is necessary before dogmatic prognostic statements can be made. Nevertheless, since its advent the prognosis for patients with choriocarcinoma has not been as grave as the outlook presented by Ewing in 1910 and reiterated by other writers as recently as 1950.

Because there are dangers in the use of methotrexate, it should be given under the strict supervision of persons acquainted with its properties. Otherwise, the patient may not benefit but may even be made worse.

REFERENCES

1. Hertig, A. T. and Sheldon, W. H.: Am. J. Obst. & Gynec. 53:1, 1947.
2. Hunt, W., Dockerty, M. B. and Randall, L. M.: Obst. & Gynec. 1:593, 1953.
3. Hertz, R. and others: J.A.M.A. 168:845, 1958.

ADDITIONAL REFERENCES

Acosta-Sison, H.: Am. J. Obst. & Gynec. 58:125, 1949.

——: Am. J. Obst. & Gynec. 69:442, 1955.

——: Am. J. Obst. & Gynec. 71:1279, 1956.

Hobbs, J. E. and Price, C. N.: Am. J. Obst. & Gynec. 39:39, 1940.

Huber, H. and Hörmann, G.: Geburtsh. u. Frauenh. 14:799, 1954.

Li, M. C., Hertz, R. and Bergenstal, D. M.: New England J. Med. 259:66, 1958.

Li, M. C., Hertz, R. and Spencer, D. B.: Proc. Soc. Exper. Biol. & Med. 93:361, 1956.

Paalman, R. J. and Vander Veer, C. G.: Am. J. Obst. & Gynec. 65:491, 1953.

Sexton, L. I., Hertig, A. T., Reid, D. E., Kellog, F. S. and Patterson, W. S.: Am. J. Obst. & Gynec. 59:13, 1950.

Smalbraak, J.: Trophoblastic Growths. Amsterdam, Netherlands, Elsevier Publishing Co., 1957.

Villee, C.: The Placenta and Fetal Membranes. Baltimore, The Williams & Wilkins Company, 1960.

Surgical Considerations of Aneurysms and Atherosclerotic Occlusive Lesions of the Aorta and Major Arteries

E. STANLEY CRAWFORD, MICHAEL E. DEBAKEY, DENTON A. COOLEY AND GEORGE C. MORRIS, JR.*

Baylor University College of Medicine, Houston

This report is an analysis of aneurysms and atherosclerotic occlusive lesions based on the treatment of 3,324 patients in the past 10 years.

Symptoms were relieved and pulses restored in 97 per cent of aorto-iliac occlusions, 90 per cent of femoropopliteal occlusions, 95 per cent of operable lesions of the internal carotid artery, and 91 per cent of vertebral arterial occlusions.

Mortality in 116 aneurysms of the descending thoracic aorta was 20 per cent, in 62 dissecting aneurysms 29 per cent, and in 829 aneurysms of the abdominal aorta 6 per cent.

RECOGNITION of the segmental nature of vascular lesions of the aorta and peripheral arteries and the development of graft replacements and technics of arterial suture have resulted in truly impressive progress during the past decade in the field of vascular surgery. Application of this knowledge has, for example, finally permitted definitive treatment of aneurysm of the aorta, a disease that has challenged physicians for centuries. Repair of these defects and replacement by graft have resulted in cure with a normal life expectancy, contrasted with the disappointment associated with earlier, purely palliative procedures. Of even more significance has been the progress made in treatment of arteriosclerotic occlusive disease, because of its vastly greater incidence. Owing to its predilection to involve and block such vital arteries as the aorta and those that supply blood to the brain, heart and kidneys, it is by far the most common cause of death and disability among vascular lesions. Recently it has become generally realized that in many forms of this disease the atherosclerotic occlusive lesion is well localized and segmental in nature with relatively normal arteries proximal and distal to the diseased vessel. This

*From the Cora and Webb Mading Department of Surgery, Baylor University College of Medicine, and the surgical services of the Jefferson Davis, Methodist and Veterans Administration Hospitals, Houston, Texas.

Supported in part by the United States Public Health Service under grants H-3137, HTS-5387 and H-4763, and by the Houston Heart Association.

E. STANLEY CRAWFORD

MICHAEL E. DEBAKEY

DENTON A. COOLEY

GEORGE C. MORRIS, JR.

concept, evolved by numerous investigators, has resulted in the development of surgical technics to remove or bypass the occlusive lesion and restore normal flow and, hence, to restore function to the distal ischemic tissues. This report is concerned with observations derived from the application of reconstructive operation in the treatment of 3,324 patients with aneurysm and atherosclerotic occlusive disease.

Atherosclerotic Occlusive Disease

The most common cause of arterial obstruction is arteriosclerosis. This disease usually involves the origin or bifurcation of arteries in characteristic locations, which are responsible for such well-known clinical entities as arterial insufficiency of the lower extremities, hypertension, cerebral arterial insufficiency, and coronary artery insufficiency. Regardless of the location of the lesion, its frequent segmental nature is now well established. From this fundamental knowledge, methods of surgical treatment have been devised to restore circulation through the normal channels. Three basic types of surgical attack have thus evolved: excision and graft replacement, endarterectomy and graft bypass. The selection of patients for operation and the application of these technics depend largely on the nature and location of the lesion.

Aorto-iliac Occlusion

This form of occlusive disease may be quite variable in its pathologic features; however, the atherosclerotic process begins with intimal proliferation and mural deposits of lipid material at the aortic and iliac bifurcations. Subsequent enlargement of this atheromatous lesion produces increasing narrowing of the lumen until a critical degree of constriction is reached which slows blood flow sufficiently to cause thrombosis and complete obstruction. When the disease progresses to obstruction of both common iliac arteries, complete occlusion of the distal aorta occurs, and the thrombus gradually propagates in a retrograde manner toward the renal arteries.

Secondary distal occlusions occur in the femoral or popliteal arteries in 25 per cent of patients with aorto-iliac occlusion. The incidence of secondary distal involvement is greater in patients with incomplete occlusion of the proximal segment. The reason for this increased incidence of distal involvement probably lies in the fact that the symptoms in these cases are due predominantly to the distal lesions, proximal obstruction being insufficient in many cases to cause significant symptoms.

Although the diagnosis of aortic and iliac arterial occlusion can usually be made on the basis of characteristic clinical manifestations of the disease, including claudication in the calves and hips, ischemic cutaneous changes in the feet and legs, and absent or diminished pulses in the femoral, popliteal and pedal regions, aortography is an important aid in planning operation. This procedure not only reveals precise information concerning the extent of the lesion both proximally and distally, but permits recognition of such associated lesions as renal and superior mesenteric arterial obstruction and distal lesions in the arterial

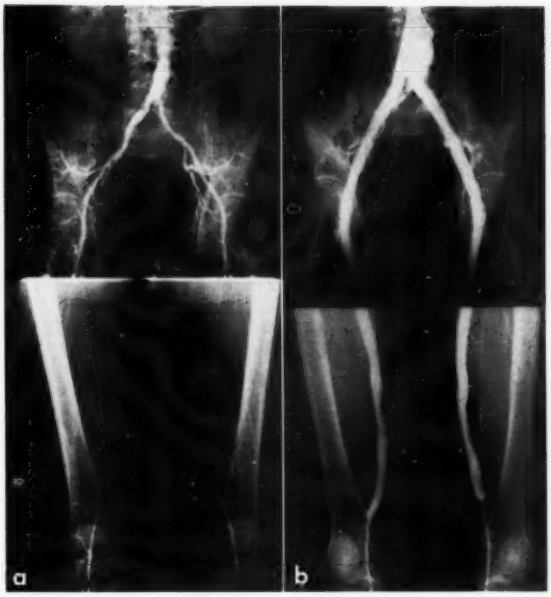


FIGURE 1. Illustrations of case in which circulation was restored with a bypass graft of DACRON®.

a. Angiogram made before operation showing partial occlusion of aorta, both common iliac arteries and left superficial femoral artery, and complete occlusion of right superficial femoral artery.

b. Angiogram made after operation showing functioning bypass graft in place extending from aorta above lesion to both common femoral and both popliteal arteries below lesion.

tree of the lower extremities. Since the occlusive process in the aorto-iliac region is almost always segmental in nature with a patent distal vessel in the pelvis, groin or popliteal region, virtually all patients are candidates for operation, although advanced cerebral or cardiac disease or other diseases severely limiting both activity and life expectancy constitute contraindications. Even under these circumstances, if the alternative is amputation, restorative operation is preferable and employed despite the increased risk. Advanced age, compensated heart disease, hypertension and diabetes are definitely not contraindications to operation, as one or a combination of these complicating factors was present in over half of our patients, yet the total over-all mortality was only 2 per cent.

The objective of treatment is to restore normal circulation to the tissues distal to the area of obstruction. This may be achieved by endarterectomy, excision and graft replacement, excision and graft replacement with bypass, end-to-side graft bypass, or a combination of these operative procedures. The type of procedure depends on the location, extent and nature of the occlusive process. Endarterectomy may be used in cases with a well-localized occlusive lesion and minimal medial and adventitious involvement. In cases with more destructive mural changes but a well-localized occlusive process, excision of the diseased ves-

TABLE 1

AORTO-ILIAC AND FEMOROPOPLITEAL OCCLUSIONS; RESULTS OF TREATMENT

TYPE	NUMBER OF CASES	SUCCESSFUL		DEATHS	
		Number	*Per cent*	*Number*	*Per cent*
Aorto-iliac	952	921	97	19	2.0
Femoropopliteal	774	653	90	3	0.4
Total	1,726	1,574	91	22	1.3

TABLE 2

AORTO-ILIAC AND FEMOROPOPLITEAL OCCLUSIONS; RECURRENT OCCLUSION AND REOPERATION

TYPE	NUMBER OF CASES	RECURRENT OCCLUSION		
		Cases	*Reoperation*	
			Number	Successful
Aorto-iliac	952	43 (4.5%)	42	39
Femoropopliteal	774	149 (19%)	107	98
Total	1,726	192 (11%)	149	137

sel with graft replacement is the operation of choice. In most cases, however, particularly in older patients and where there is extensive atheromatous disease with partial or complete obstruction of long vascular segments, the bypass graft procedure is considered preferable because it permits operation with minimal dissection (figure 1).

The results of operation in 952 cases with occlusion of the aorta and iliac arteries were highly gratifying. Restoration of pulses and relief of symptoms were obtained in 97 per cent of the cases with a mortality of 2 per cent (table 1). Follow-up studies on this group of patients extending for periods of over five years have also been encouraging in that recurrent occlusion was encountered in only 43 patients (4.5 per cent) in this series. Successful restoration of circulation was achieved by a second operative procedure using a bypass graft in 39 of the 42 patients submitted to reoperation (table 2).

Femoropopliteal Occlusions

Femoropopliteal occlusions may also be variable in location but generally may be classified into one of three types. The lesion (1) may be quite discrete and localized to a very short segment of artery with normal vessel above and below the obstruction, (2) may be more extensive with involvement of a considerable portion, if not all, of the superficial femoral artery but with patency of the popliteal artery and distal arterial bed, or (3) may involve any portion of the artery above in addition to the popliteal artery and extend well down into the small vessels of the calf without a distal segment of sufficient size to attach a graft. The latter type is inoperable. Severe peripheral ischemia is more likely to be associated with occlusions of the third type, while intermittent claudication limited to the calf and foot is more often associated with the first and second types of lesion. The extent or location of the lesion cannot, however, be predicted with sufficient accuracy on clinical grounds alone; arteriographic visualization is necessary for adequate localization of the lesion. Because of the frequency of unsuspected proximal partial occlusions in the aorto-iliac area, we prefer to visualize the entire arterial tree from abdominal aorta to popliteal runoff rather than limit the examination to femoral arteriograms (figure 1).

Treatment in this series of cases was directed toward restoration of normal pulsatile circulation, an approach that could be applied in 90 per cent of the patients with claudication and good circulation at rest and in 50 per cent with more advanced manifestations of arterial insufficiency. The procedures mentioned earlier are again applicable, although in our present series of 774 cases the occlusion was well localized to a short segment and suitable for endarterectomy in only 4.4 per cent (figure 2). Except in cases with an associated aneurysm of the femoral or popliteal artery, excision and graft replacement (used in 2.4 per cent of our earlier cases) has been abandoned because of certain disadvantages, chief of which is the destruction of collateral circulation. The bypass graft procedure, which has the advantage of not altering the blood flow in the patient's collateral vessels, was used in the vast majority of cases and is considered the procedure of choice (figure 1).

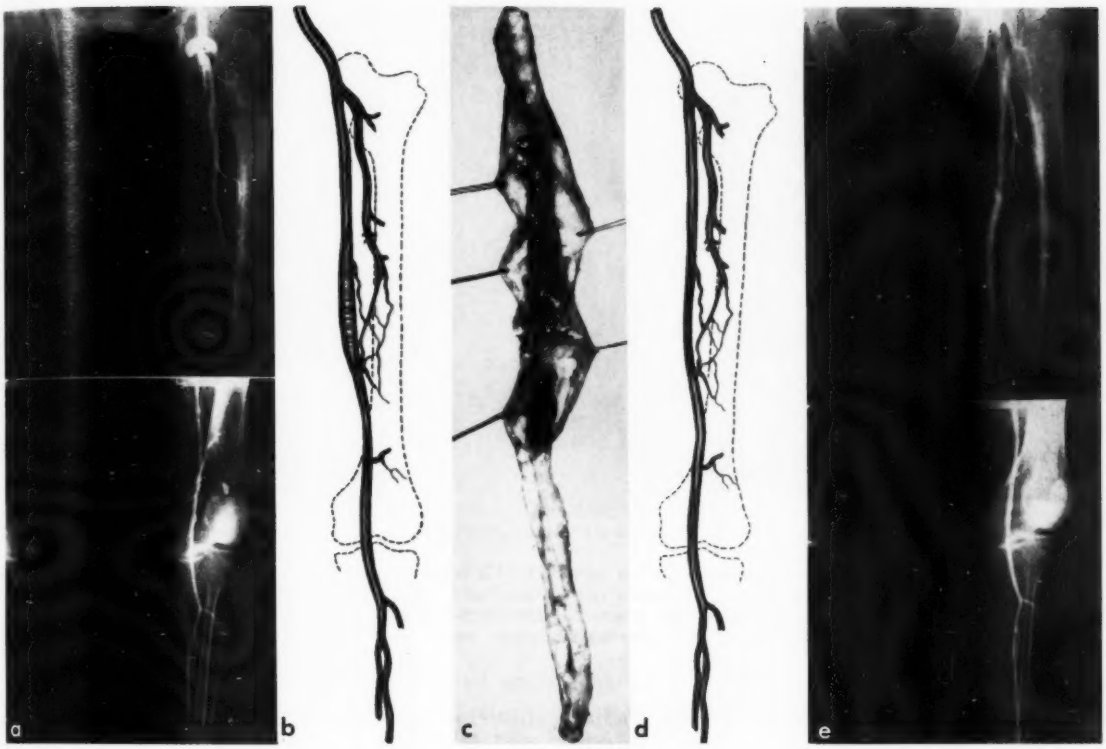


FIGURE 2. Illustrations demonstrating preferred method of endarterectomy, a procedure limited to short occlusions.
a. Arteriogram made before operation showing segmental occlusion of superficial femoral artery.
b. Diagram showing extent of occlusion (darker area).
c. Photograph of specimen removed at operation showing thrombus superimposed on atheromas.
d. Diagram showing longitudinal arterial incision repaired using patch graft.
e. Arteriogram made after operation showing reasonably normal vascular channels.

Excellent results with restoration of a normal distal pulsatile blood flow and relief of symptoms have been obtained in 90 per cent of these cases (table 1). Recurrent obstruction has developed in 19 per cent because of progression of the proximal or distal disease or as a result of technical factors, but in 98 out of 107 patients submitted to reoperation for recurrent obstruction the presence of a patent distal segment permitted restoration of a normal pulsatile circulation (table 2).

Innominate, Carotid, Subclavian and Vertebral Arterial Occlusion

Occlusive disease of these arteries tends to assume one of two patterns, proximal or distal, although multiple lesions may frequently be seen. The proximal lesions, located at or near the origins of the great vessels arising from the aortic arch, result in arterial insufficiency of the cerebrum and upper extremities, and although they may be either well localized or extensive a patent accessible distal segment is always present. Pulses may be diminished or absent in the neck and arms, the blood pressure may be different in the two upper extremities, and systolic murmurs may be present in the base of the neck. The distal forms of the disease, located at the origins of the vertebral and internal carotid arteries, result in attacks of cerebral artery insufficiency that may be transient, apoplectic or

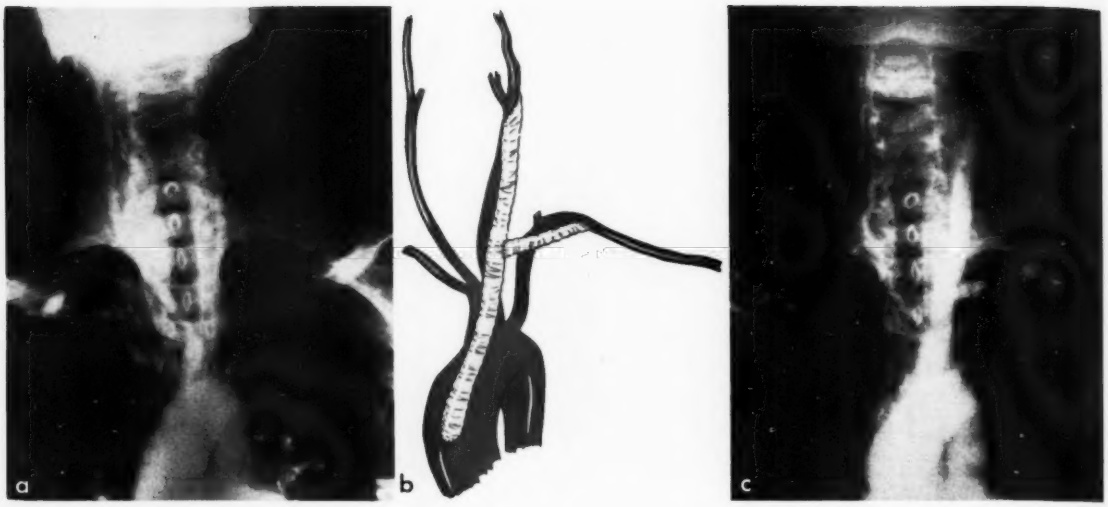


FIGURE 3. Illustrations demonstrating use of bypass graft in treatment of occlusion of left common carotid and left subclavian arteries.

a. Angiogram showing occlusion of left carotid and left subclavian arteries.

b. Diagram showing extent of occlusion (darker area) and bypass graft extending from ascending aorta proximally to subclavian and left common carotid arteries distal to occlusion.

c. Angiogram made after operation showing functioning bypass graft in place.

progressive. Patients with occlusion of the internal carotid artery usually have contralateral motor and sensory disturbances and homolateral monocular visual symptoms. Occlusions of the vertebral arteries are associated with symptoms ascribed to basilar artery thrombosis, i.e., bilateral visual disturbances, vestibular dysfunction, ocular nerve defects, and bilateral motor and sensory disturbances. Although murmurs are often present in the neck, diagnosis depends on arteriographic demonstration, as clinical differentiation between intracranial and extracranial occlusions is not possible with any consistent accuracy. In our experience, 40 per cent of all patients with cerebral arterial insufficiency examined arteri-

TABLE 3

OCCLUSIVE DISEASE OF INNOMINATE, CAROTID, SUBCLAVIAN AND VERTEBRAL ARTERIES; LOCATION OF LESIONS IN 208 PATIENTS

LOCATION	NUMBER OF LESIONS	EXPLORED		CIRCULATION RESTORED	
		Number	*Per cent*	*Number*	*Per cent*
External carotid	9	9	100	8	89
Internal carotid	256	211	82	185	88
Common carotid	16	16	100	16	100
Innominate	16	15	94	15	100
Subclavian	29	27	93	27	100
Vertebral	55	32	58	29	91
Total	381	310	81	280	90

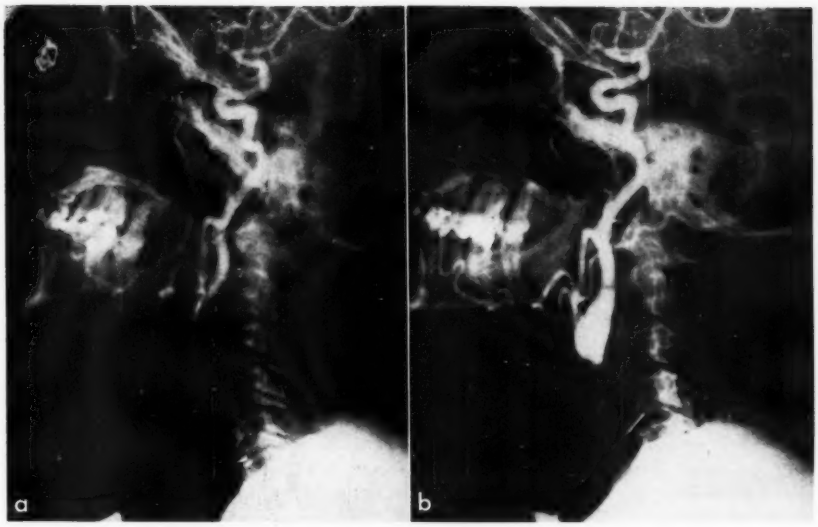


FIGURE 4. Illustrations of patient with partial occlusion of left internal carotid artery treated by endarterectomy and patch graft repair.
a. Arteriogram made before operation.
b. Arteriogram made after operation.

ographically had significant extracranial arterial disease.

Surgical treatment is directed toward restoration of circulation to relieve symptoms and prevent progression of the disease. Lesions of the great vessels arising on the aortic arch are usually more extensive and are preferably treated by the bypass technic, whereas the distal lesions, when operable, are usually discrete and well localized and are treated by longitudinal arteriotomy, endarterectomy, and closure of the vessel using an elliptic patch of knitted Dacron to prevent narrowing by the suture of these small arteries (figures 3 and 4). Temporary shunts are used to maintain the distal circulation during operation in cases with contralateral occlusion or with inadequate collateral circulation.

Of 310 lesions in 208 patients submitted to operation in the past six years, circulation

TABLE 4

OCCLUSIVE DISEASE OF INNOMINATE, CAROTID, SUBCLAVIAN AND VERTEBRAL ARTERIES; TYPE OF OCCLUSION IN 208 PATIENTS

TYPE OF OCCLUSION	NUMBER OF LESIONS	EXPLORED		CIRCULATION RESTORED	
		Number	*Per cent*	*Number*	*Per cent*
Proximal					
Complete	29	28	97	28	100
Incomplete	32	30	94	30	100
Distal					
Complete	64	29	45	10	34
Incomplete	256	223	87	212	95
Total	381	310	81	280	90

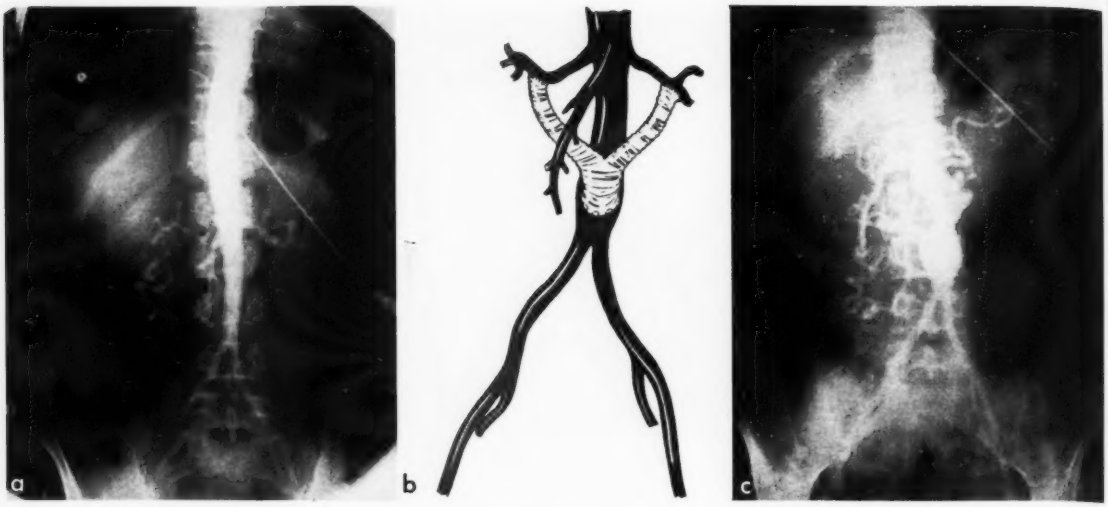


FIGURE 5. Illustrations of patient with bilateral partial occlusion of renal arteries demonstrating treatment with bypass Dacron graft.

a. Aortogram made before operation showing partial occlusion of both renal arteries.

b. Diagram showing extent of occlusion (darker area) and bypass graft extending from aorta proximally to renal arteries distal to occlusion.

c. Aortogram made after operation showing bypass graft in place.

was restored in all patients with lesions involving the great vessels, 95 per cent of those with operable lesions of the internal carotid artery, and 91 per cent of those with vertebral arterial occlusion (tables 3 and 4). Follow-up over a five year period has shown that the success of the operation has been well maintained with recurrence in only four patients.

Renal Arterial Occlusion

Renal arterial occlusion is one of the main causes of hypertension in patients with arteriosclerosis. The atherosclerotic occlusive lesion in these cases is usually located near the origin of the renal arteries and involves only a few centimeters of the vessel wall with a relatively normal patent lumen distally. It may be unilateral or bilateral, complete or incomplete. The absence of other causes of hypertension and the presence of atherosclerosis elsewhere suggest the possibility of renal arterial occlusion. The diagnosis is made by aortography as done for aorto-iliac disease (figure 5).

Treatment depends on whether the lesion has produced complete or incomplete obstruction. In incomplete obstruction, any one of the previously described procedures can be used to restore normal pulsatile flow to the kidney, whereas nephrectomy is usually required for the cases with complete renal arterial obstruction (figure 5). Results of these methods of treatment have been most gratifying, with disappearance or relief of the hypertension in almost all of the 46 patients in this series in whom arterial reconstructive procedures were employed for renal arterial occlusion.

Aneurysm

Aneurysms may be classified etiologically into congenital and acquired types, or morphologically into sacciform, fusiform and dissecting types. Sacciform aneurysms involve only a part of the aortic circumference, and the aneurysmal sac made up of a pouchlike dilatation of the localized weakened area of aortic wall is attached to the uninvolved vessel by a narrow neck. Fusiform aneurysms are spindle-shaped and involve the entire circumference of vessel wall. Dissecting aneurysms

are of intramural origin and are characterized by a hemorrhagic intramural separation of the aortic wall which communicates with the normal lumen by an intimal tear.

The essential factor in the pathogenesis of aneurysm is a medial disruptive process, whether it results from trauma, infection or atherosclerosis, and progressive dilatation occurs at the weakened area. Nature's attempt to counteract this pathologic process consists of the development of fibrous tissue around the aneurysm and the laying down of laminae of thrombi on the inner surface of the sac wall. These efforts are at best inadequate, and the continuous pounding of the blood and the fact that fibrous tissue is an unsatisfactory replacement for elastic tissue result in progressive stretching and thinning of the wall. Ischemic liquefaction instead of organization of the laminated thrombus occurs in addition, resulting in progressive enlargement and ultimate rupture.

Aneurysms of the thoracic aorta, once considered predominantly syphilitic, are now known to be frequently arteriosclerotic in origin. Syphilitic aneurysms are usually saccular, and arteriosclerotic aneurysms are usually fusiform in nature. In the abdominal aorta, the aneurysms are predominantly arteriosclerotic and fusiform and characteristically arise just below the origin of the renal arteries. Dissecting aneurysms result from degeneration of elements of the media, but this is apparently unrelated to syphilis or arteriosclerosis. According to the prevailing hypothesis, the lesion begins as an intramural hematoma from rupture of the vasa vasorum with secondary rupture of the intima. The dissection follows the tear in the intima and commonly begins a few centimeters above the aortic valve or in the descending thoracic aorta near the origin of the left subclavian artery, and a forceful stream of blood dissects down the media. The dissection shears off small branches when encountered or dissects out larger arteries for varying distances, often closing the orifices of these vessels. The end result is usually rupture into the pericardium, mediastinum or pleural cavities. In chronic forms the defective passage may re-enter the aortic lumen to decompress the process and form a double-barreled aorta.

The clinical manifestations of aneurysm vary considerably with the location and extent of the lesion, but unlike the peripheral arteries where thrombosis and peripheral ischemia are common manifestations, obstruction of blood flow rarely results except in those aneurysms in the distal abdominal aorta. In the early stages of almost all aneurysms, they are asymptomatic and may obtain full development without causing significant objective symptoms until fatal rupture occurs. Signs and symptoms usually result from encroachment on adjacent structures. In the thoracic aorta, compression of the vena cava and innominate veins produces venous distention and edema of the head and neck. Dyspnea and cough result from compression of the air passages, and death by suffocation is not uncommon. Hoarseness may be produced by pressure on the recurrent laryngeal nerve. Erosion of the sternum and ribs may occur in aneurysms of the ascending aorta or the aortic arch, and aneurysms of the descending aorta may erode vertebrae. An aneurysm of the abdominal aorta may be noted as a pulsating abdominal mass accompanied by varying degrees of discomfort. Pain is a particularly ominous sign as it often represents rapid enlargement and may signify imminent or actual rupture of the aneurysm with retroperitoneal extravasation of blood. The most important physical finding is the presence of an expansile pulsating mass at the level of the umbilicus.

The diagnosis of aortic aneurysm is not difficult, although in the chest, where transmitted pulsation from the ventricles may simulate actual pulsation, it may be difficult to differentiate from a solid tumor. Angioaortography here is often a valuable means of diagnosis, although false negative results may occur in saccular aneurysms filled with clot. With abdominal aneurysms, aortography is rarely necessary as it is usually possible to demonstrate the aneurysm in plain roentgenograms of the abdomen, particularly in the lateral or oblique projection, because of calcification in the wall. The most important factor in the diagnosis of dissecting aneurysm is

awareness of its occurrence, particularly in the presence of the characteristic clinical manifestations. The most striking manifestation of this disease is the sudden onset of severe, almost indescribable pain in the chest or epigastrium, which may extend along the course of the ribs to the back, then up into the neck and shoulders or down into the abdomen. The symptoms may be less severe but exhibit "marching" of manifestations from one region to the other as the dissection progresses down the aorta. The most common finding on roentgenograms of the chest is widening and radiolucency of the aortic arch and descending thoracic aorta. A double aortic shadow with a somewhat dense central core and a more radiolucent outer portion representing the dissected passage is common. Angiocardiography emphasizes this contrast and is probably the most valuable diagnostic procedure.

The serious prognosis of aneurysmal disease of the aorta has long been recognized. In dissecting aneurysm it is extremely grave, with death occurring within 24 hours of onset in 58 per cent and from one day to one week in 26 per cent of Shennan's series. Only 10 to 15 per cent of patients with the chronic or healed type of dissection have a significant chance of survival. In 1,113 patients with other types of aneurysms of the thoracic aorta, analyzed by Kampmeier, the average duration of life after onset of symptoms was six to eight months. In our series of 97 patients with aneurysms of the thoracic aorta observed before the advent of corrective operation, 91 patients died during the five year period following diagnosis. The average duration of life in patients with aneurysms of the abdominal aorta is somewhat longer, but the prognosis is also grave. Estes found in his analysis of 102 patients with this condition that one-third were dead within a year of diagnosis, one-half within three years, and three-fourths within five years, usually from rupture. Wright, in his follow-up study of 68 cases, found only 4 per cent of the patients had survived for five years.

The treatment of aneurysm requires extirpation of the lesion and restoration of normal vascular continuity. In dissecting aneurysms, if the lesion begins in the ascending aorta, a re-entry from the false to the true aortic lumen is created by dividing the descending aorta between clamps and creating an aortic window above, obliterating the false lumen below, and restoring continuity with end-to-end anastomosis. Where the dissection begins distal to the subclavian artery, the involved descending aorta can be resected and replaced with a graft. In sacciform aneurysms, extirpation of the lesion may be possible by tangentially clamping the aorta across the neck of the sac, excising the wall of the aneurysm, and performing lateral aortorrhaphy. Larger saccular aneurysms and fusiform aneurysms require isolation of the involved segment of aorta and maintenance of circulation distally to prevent heart strain and ischemia to sensitive tissues, particularly the brain and spinal cord. This can be accomplished by any one of a number of internal or external shunting procedures. Following isolation of the involved segment, resection and replacement by a vascular prosthesis can be performed (figure 6). In aneurysms below the renal arteries, direct occlusion above and below the involved area can be done with resection and replacement of the diseased aorta without the necessity of shunting procedures (figure 7).

The results of these methods of excisional therapy have been most gratifying and support the conviction that they provide the most effective form of management for this disease (table 5). The operative mortality varies with the type and location of the lesion and is particularly influenced by certain factors such as advancing age, pre-existing heart disease, and acute rupture. The influence of age is shown by the fact that the operative mortality among patients in the eighth decade of life is twice that of the fourth and fifth decades. Similarly, the fatality rate among patients with pre-existing heart disease is more than three times greater than that among patients without heart disease. Our mortality in 116 cases of aneurysm of the descending thoracic aorta was 20 per cent, in 62 cases of dissecting aneurysms 29 per cent, and in 829 aneurysms

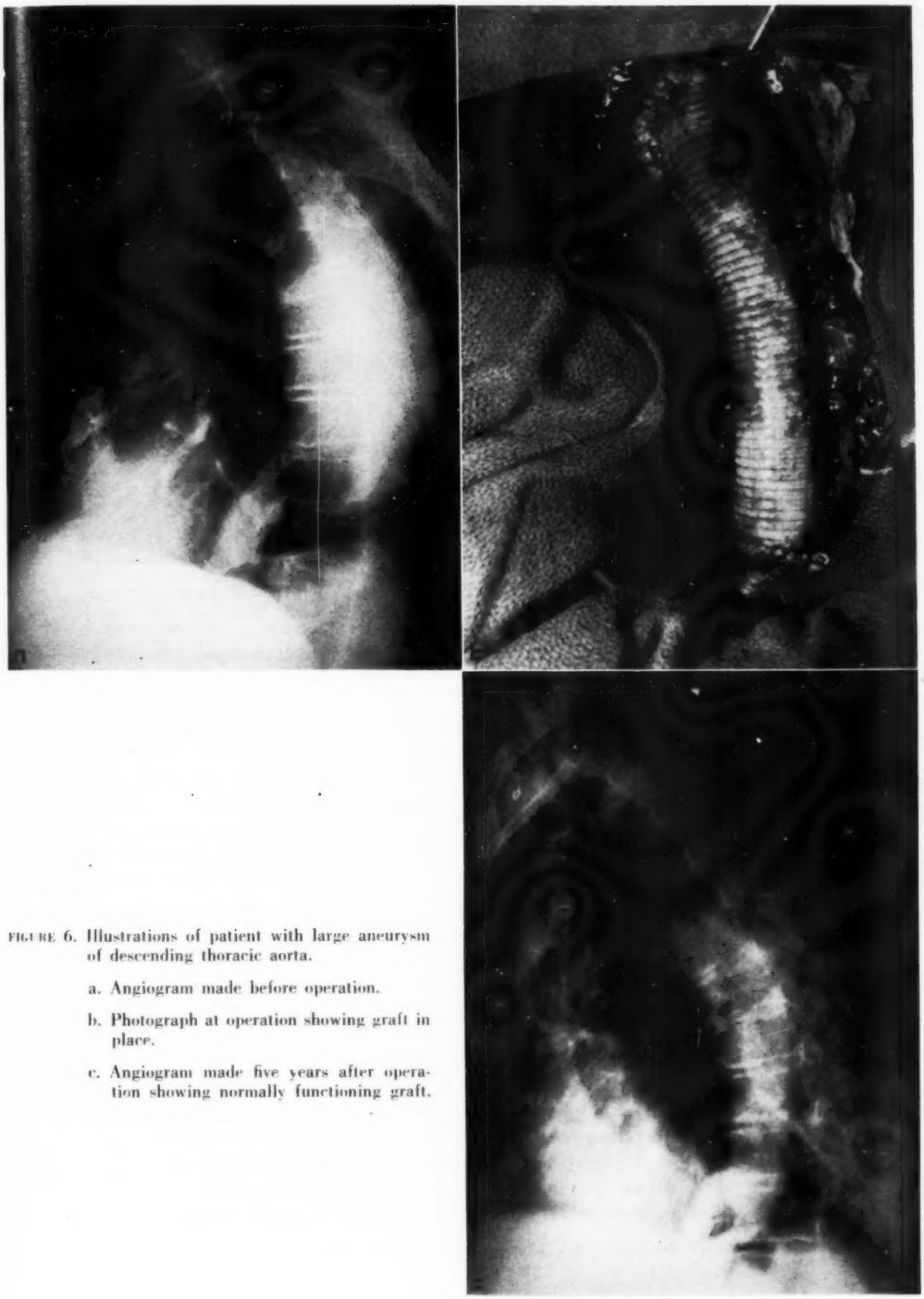


FIGURE 6. Illustrations of patient with large aneurysm of descending thoracic aorta.

a. Angiogram made before operation.

b. Photograph at operation showing graft in place.

c. Angiogram made five years after operation showing normally functioning graft.

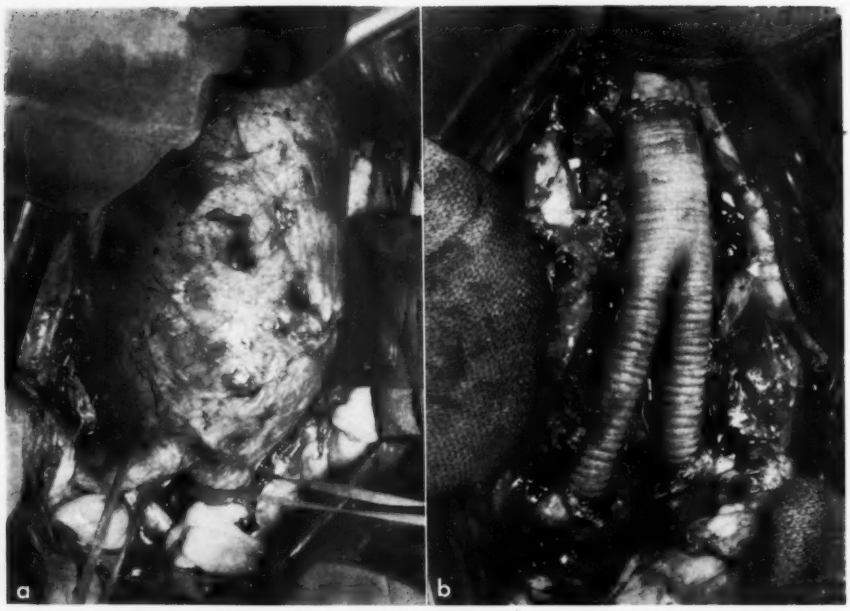


FIGURE 7. Illustration of case showing excision and graft replacement of abdominal aortic aneurysm.
a. Photograph at operation showing large abdominal aortic aneurysm with normal segments above and below.
b. Photograph at operation showing Dacron graft in place.

of the abdominal aorta 6 per cent. Finally, the studies of the long-term results of operation with follow-up observation extending over a period of five years reveal a significant increase in life expectancy in the operated versus the nonoperated group. Sixty-two per cent of our patients with abdominal aneurysm treated surgically were alive at the end of five years versus 10 per cent in the nonoperated series of Estes and Wright.

Summary

In the past decade, impressive advances have been made in the field of vascular sur-

TABLE 5

ANEURYSMS OF AORTA AND PERIPHERAL ARTERIES; 1,242 PATIENTS

LOCATION	NUMBER OF CASES	DEATHS	
		Number	*Per cent*
Aortic arch	56	31	55
Descending thoracic aorta	116	23	20
Dissecting aneurysm	62	18	29
Thoracoabdominal	25	8	32
Abdominal	829	51	6
Peripheral artery	154	4	3
Total	1,242	135	11

gery. The development of blood banking, technics of arterial suture, and arterial graft replacement combined with the concept of localization of segmental involvement of vascular lesions have permitted truly remarkable progress in arterial surgery. Several methods of surgical treatment have been developed which may be employed in accordance with the nature of the lesion to restore normal circulation. This report is an analysis of our experience in the diagnosis and treatment of 3,324 cases in the past 10 years.

The location and extent of the occlusive process in atherosclerotic obstructive lesions tend to assume certain recognizable patterns. Among these, the most important from a surgical standpoint are those involving the aortoiliac region and the femoropopliteal region, which result in ischemic manifestations in the lower extremities; those involving the renal arteries, producing hypertension; and those involving the innominate, carotid, vertebral and subclavian arteries, causing arterial insufficiency of the brain and upper extremities. As the atherosclerotic process is frequently well localized and segmental in nature with a relatively normal vessel proximal and distal to the lesion, surgical treatment can be applied to restore normal flow to the ischemic tissues distal to the area of obstruction. This therapy can take the form of one of three basic procedures: endarterectomy, excision and graft replacement, and the bypass graft procedure. As applied to thrombo-occlusive disease, the results have been most gratifying, with relief of symptoms and restoration of pulses in 97 per cent of the cases with aortoiliac occlusion, 90 per cent of the cases with femoropopliteal occlusion, 95 per cent of those with operable lesions of the internal carotid artery, and 91 per cent of those with vertebral arterial occlusion.

With the exception of dissecting aneurysms originating from the ascending aorta, which are currently treated by a decompressive procedure, nearly all aneurysms of the thoracic and abdominal aorta and peripheral arteries are technically amenable to excisional therapy with repair of the defect by suture or by replacement with a prosthesis. The results again have been most satisfactory, and with the advancement of technics have been associated with a constantly decreasing operative mortality. Our mortality in 116 cases of aneurysms of the descending thoracic aorta was 20 per cent, in 62 cases of dissecting aneurysms 29 per cent, and in 829 patients with aneurysms of the abdominal aorta 6 per cent. The follow-up observations over a five year period show a significant increase in life expectancy following excision and graft replacement in patients with abdominal aortic aneurysm, with 62 per cent of our surgically treated group alive at the end of five years versus 10 per cent of a comparable group not treated by surgery.

Postgraduate Clinical NOTES

154. ENZYME DEFICIENCIES

An increasing variety of disorders associated with a metabolic block and recessive inheritance has been discovered. Although rare, it is important to recognize these early since, in a number, prompt treatment will prevent mental impairment and other pernicious effects. An enzyme defect may provoke mental disorder either through the accumulation of toxic metabolites in grossly abnormal amounts or through the absence of an end-metabolite which is essential for normal development.

Bernard Schlesinger, Advances in paediatrics, *The Practitioner*, October 1960, pp. 429-430

The Subcuticular Suture

RICHARD E. STRAITH, JAMES M. LAWSON AND C. JACK HIPPS*

The Straith Clinic, Detroit

The use of large interrupted sutures in facial skin is not justified and should be condemned. Routine use of silk and catgut sutures in facial wounds is contraindicated. The authors present a modification of Halsted's subcuticular suturing technic employed at the Straith Clinic and describe a method of acquiring skill in its performance before attempting the closure of facial wounds. They believe this technic is greatly superior to any other method of closure of facial wounds.

THE economic importance of a fine suturing technic can be realized when one considers that millions of dollars in insurance claims are awarded annually to the victims of automobile accidents on the basis of their unsightly scars. Juries also have been known to award claims to plaintiffs in malpractice suits where the issue was solely that of a conspicuous scar left by the surgeon. Other considerations of equal importance to the surgeon, of course, are the satisfaction of a job well done and the happiness of his patient.

RICHARD E. STRAITH

This presentation is concerned largely with the primary treatment of facial lacerations. Excisions of scar tissue and other facial deformities, while often done by the plastic surgeon, are performed largely by other surgeons. Anyone who may be called on to perform such surgical procedures should have a thorough knowledge of the technic of plastic wound closure. This technic can be readily learned and results perfected with practice on animal tissue.

Probably the greatest single advance in skin-suturing technic was Halsted's development of the subcuticular suture. This was still further refined by Dr. Claire L. Straith to the technic which has been used in the Straith Clinic for almost 20 years.

The improvement in results by this method is severalfold. There are no stitch marks. The end result is a scar which is usually hairline

*The Straith Clinic for Plastic, Reconstructive and Hand Surgery, Detroit, Michigan.

Presented before the forty-fifth annual Assembly of the Interstate Postgraduate Medical Association at Pittsburgh.

JAMES M. LAWSON

C. JACK HIPPS

in width and free of depression or stretching. In potentially infected facial wounds, this suture is especially indicated because there are no superficial stitches to become infected and leave scars. The abundant blood supply plus the use of antibiotics make serious wound infections no longer a problem.

Practice Technic

To perfect the technical skill necessary to accomplish this type of closure, one of us (J.M.L.), while in training under the late Claire L. Straith, began to practice on grapefruit skin. His voluble complaints about the limitations of this material prompted his wife to search through the local grocery store for a more suitable material. She chose pigs' feet for an experiment. This immediately proved to be an ideal choice since the elasticity, thickness, toughness and needle-penetrating properties of this tissue very closely approximate those of human skin. Its cheapness and availability are other obvious advantages. Numerous closures can be accomplished on a single pig's foot (figure 1).

Since the inception of this training adjunct, every trainee of the Straith Clinic is required to become proficient in the technic prior to closing human skin. Residents and interns from other hospitals have been given only one hour of instruction with such gratifying results that we feel this training method should be included in all residency training programs.

Operative Procedure

Preparation—Thorough scrubbing with pHISOHEX® soap for a minimum of five minutes should be done for a distance of at least 15 cm. around the operative site. No alcoholic or ketonic solutions should be applied after this scrub, as they will disrupt the protective soap film; if used at all for cleansing purposes, they should be used prior to the soap cleansing. Aqueous antiseptic solutions such as ZEPHIRAN® may be used following pHisoHex preparation. Careful draping of the patient should be observed, of course, with all rigorous precautions.

Anesthesia—All attempts should be made to prepare the patient psychologically for surgery. In the absence of contraindications, the following regimen is usually employed: NEMBUTAL®, 1.5 to 3 gr., one hour preoperatively; DEMEROL®, 50 to 100 mg., one-half hour preoperatively. The dosage of these medications depends on the patient's age, weight and temperament. The common error is to give too little medication; if this is at all evident, additional intravenous Demerol is given when the patient is on the operating table.

Wherever possible, local anesthesia is used. Routinely, the smallest-caliber needle possible is employed—25 gauge usually, 2 to 3 in. in length—and, if possible, the entire area is infiltrated through one "pinprick" (very important to patients!). Where there is an open laceration, the needle can be introduced directly into the subcutaneous tissue for infiltration anesthesia, eliminating even one "pinprick" (figure 2).

XYLOCAINE® 1 per cent with ADRENALIN® in a dilution of 1:50,000 or 0.5 cc. to the ounce has been found most satisfactory. When more than an ounce of solution is used, only 0.25 cc. epinephrine per 30 cc. is used.

Scar tissue requires considerably longer to anesthetize than other tissues. At least five minutes should elapse before commencing surgery. A safe rule is to wait until the tissues begin to blanch from vasoconstriction. The presence of cardiac disease or hypertension rules out the use of epinephrine, of course. Wherever possible, block anesthesia should be used first.

Reassurance and sympathy should never be underestimated as adjuncts of chemical anesthesia. Proper decorum in the operating room

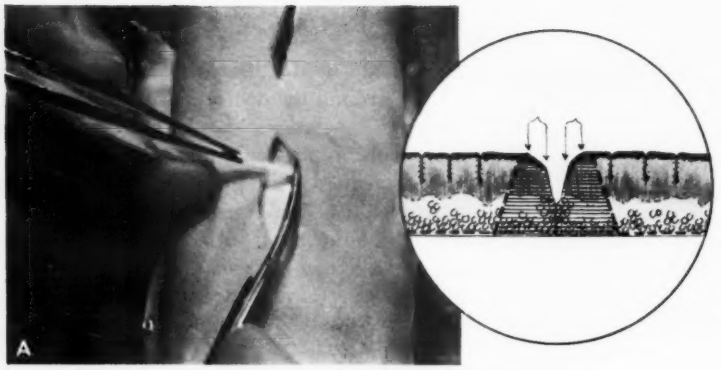
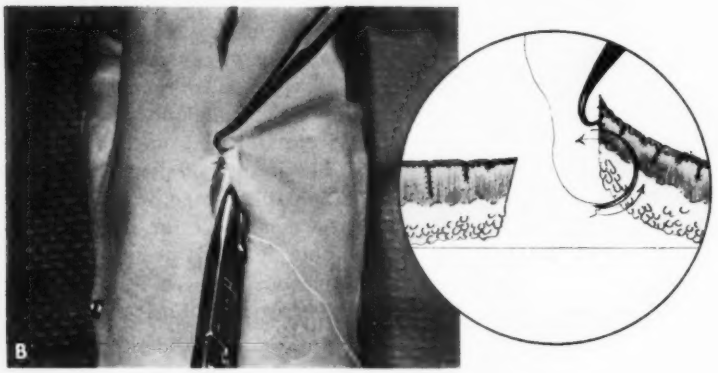
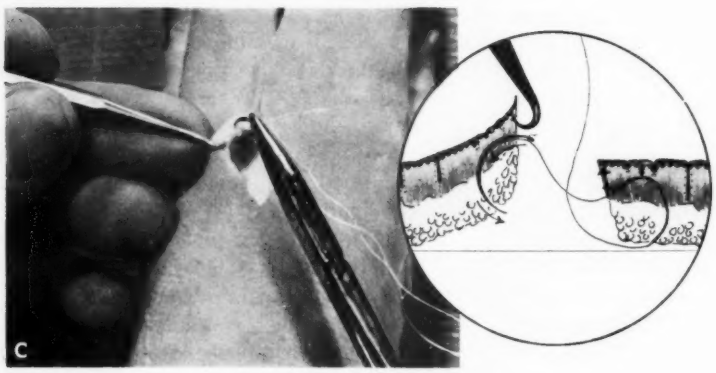


FIGURE 1. Straith Clinic skin-closure technic as practiced on a pig's foot.

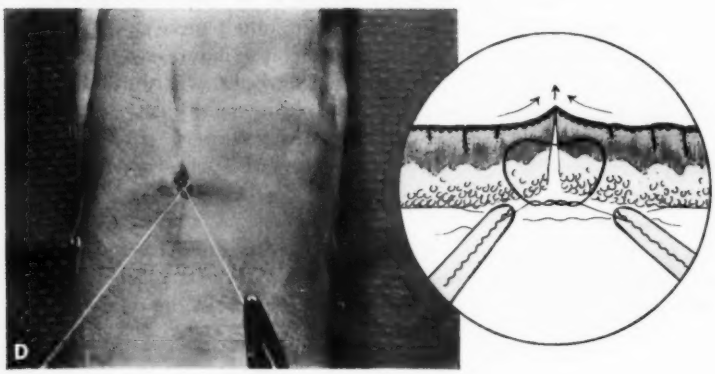
A. Bruised skin edges are excised by sharp dissection. The skin is undermined above the fascia. Tissue in the shaded area of the drawing is excised by scissors as shown in the photo to force the skin edges to evert when they are sutured together.



B. Buried *permanent* white nylon or DACRON® suture passing up through "near skin edge." Note that suture emerges from the near skin edge at a *lower* level than the highest path of the needle.

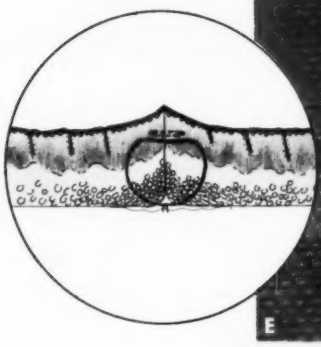


C. Same suture entering through the far skin edge. The path of the suture is a mirror image of the opposite side and emerges above the fascia in the undercut area.

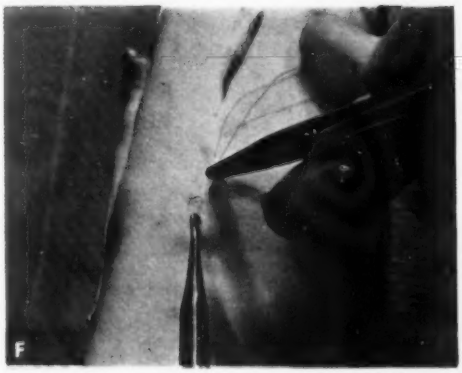


D. The first knot is a double-hitch knot to prevent slipping. Picture shows eversion of skin edges over the previous buried sutures.

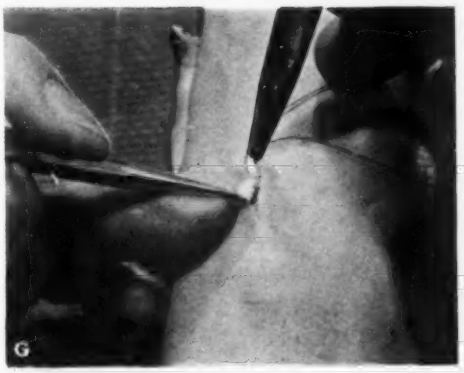
E. Projected path of 5-0 monofilament nylon suture lying above the level of the buried white nylon sutures.



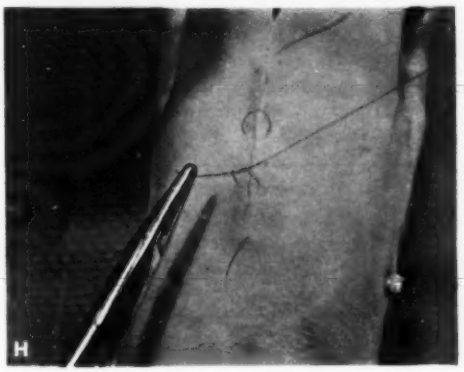
F. Entrance and exit of the suture path of each "bite" are at a lower level than the lateral portion and cause further eversion of the skin edges (see inset, figure 1E). Positioning of skin edge with a fine hook and the holding of the needle holder as one holds a pen are absolutely essential.



G. Accurate apposition is insured by slight "backtracking" of each "bite" (see projected path, figure 1E). The exit of the previous stitch and the entrance of the opposite stitch are at the same level. Again, "pen grasp" of the needle holder is *essential!*



H. Occasionally, a first half of a surgeon's knot is left in place for 48 hours for more accurate closure. Note the "surfacing" loop of continuous monofilament nylon in the center of the wound after every ¾ in. of closure. The loops are cut after two to three weeks and sutures are removed in sections.



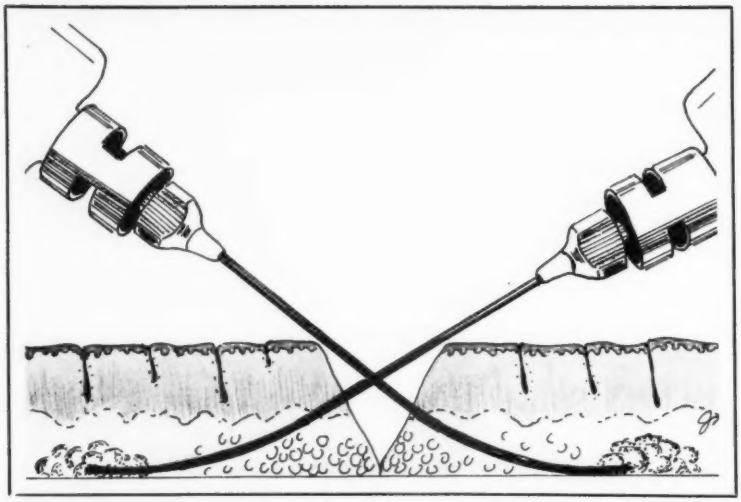


FIGURE 2. To minimize pain and fear, the needle is always introduced through the open wound edges, which are always cleaner than the skin.

FIGURE 3. Langer's lines, showing the direction of ideal excisions. These vary somewhat from patient to patient.

is also indispensable for maximal anesthesia.

Operative technic—Wherever possible, skin incisions should be made in the normal tension lines and never at right angles to them. These lines, known as Langer's lines, are shown in figure 3 with typical incisions. This will insure the least possible scar spreading. In lacerations, the direction of the incision already is established, although it may be changed if alteration does not lengthen it unduly.

Incisions must be made sharply, with skin edges slightly overhung from 90 degrees (figure 1A). In cases of lacerations, debriding of all skin edges must be similarly done. Usually, 1 to 2 mm. of normal-appearing skin is sacrificed by this method. The healing properties and bacterial resistance of the wound edges have been appreciably impaired by the original trauma and usually are too uneven to allow clean, sharp approximation without debriding (figure 4).

Sufficient undercutting must be done to overcome undue tension and provide room to

FIGURE 4. Area of debridement around laceration, removing no more than 1 to 2 mm. of normal skin.

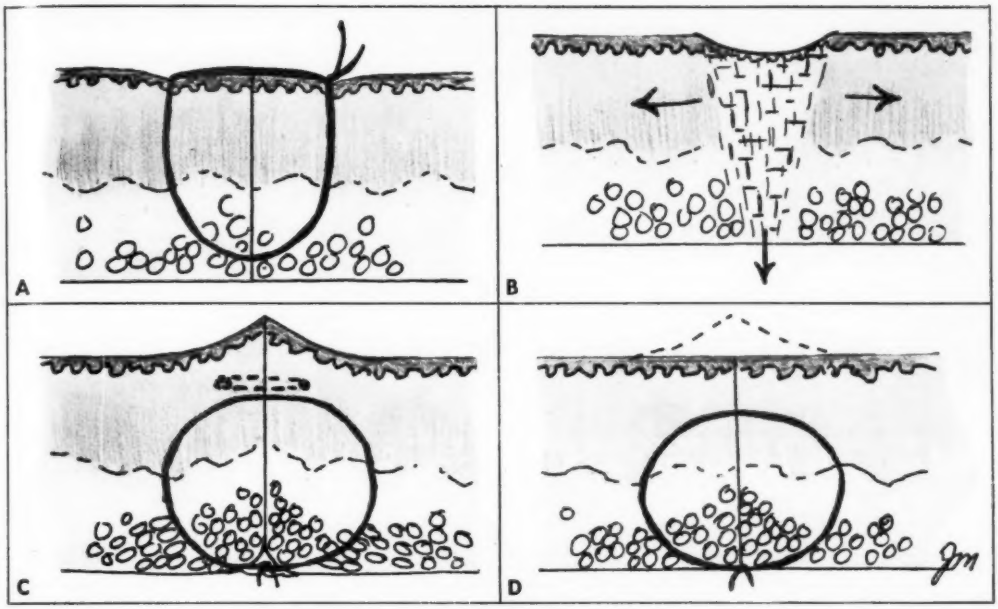


FIGURE 5. A. Usual one-layer closure.
B. Three months later, after contracture and spreading of scar.
C. Buried two-layer plastic closure with eversion of skin.
D. Three months later, after contracture, showing leveling of skin edges without spreading. Subcuticular suture has been removed.

insert the buried white nylon sutures. In many cases, much more undercutting must be done on one side than on the other. For example, around the eyes, nose or mouth, distortion can easily result if too much tissue is taken from the side of the orifice. All excess fatty and subcutaneous tissues are then carefully trimmed from the edges so that they will not intervene between the edges of the skin and thus prevent the desired eversion (figure 1A). This eversion is what prevents scar spread as the tissues contract in healing (figure 5). A layer of buried white nylon sutures is used to approximate the deeper layers of the dermis in eversion. These are placed approximately 3 to 5 mm. apart, depending on the amount of tension that must be overcome (figure 1B, C, D). An intracuticular 5-0 or 4-0 monofilament nylon suture on an Atraumatic needle is then placed through the more superficial dermal layers to better approximate and further evert the skin edges (figure 1E, F, G). It is brought out to the surface each ¾ in. to facilitate later removal (figure 1H). This is left in place for 10 to 14 days. Small interrupted sutures tied with only the first half of a surgical knot are used where any area needs better approximation. These are removed in 48 hours. Excess skin bunched around the ends of incision closures can cause elevations commonly called "dog ears." Lengthening of

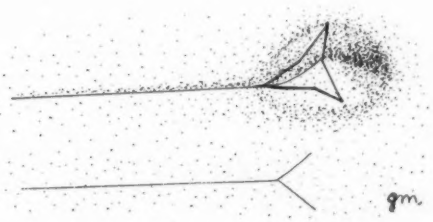


FIGURE 6. Drawing showing typical "dog's ear" at the end of the elliptic excision. Condition corrected by removal of skin as indicated and closure as a Y.

FIGURE 7. A. Scar contracture one year following closure of laceration elsewhere by interrupted suture method.

B. Eight months following scar excision and plastic closure with eversion of skin edges. When a scar crosses Langer's lines, small Z-plasties are often necessary to get the best results.

FIGURE 8. A and B. Typical scar contracture six months following interrupted suture method.

C. Two months following plastic closure. Eversion still present in cheek portion of scar.

D and E. Scars one year postoperatively. Complete flattening without spreading.

FIGURE 9. A. Eleven days after injury. Lacerations closed elsewhere with only interrupted sutures. Note crusting along wound edge from use of dry dressing, which often prevents absorption of blood.

B. Three months after injury. Inevitable contraction and spreading of all deep lacerations closed by only interrupted sutures.

C. Fifteen months following excision and two-layer plastic closure with eversion of skin edges.

FIGURE 10. A. Two months following closure of lacerations elsewhere with interrupted sutures.

B. Duke's Elastoplast No. 204 makes an ideal dressing for lacerations. Antibiotic (streptomycin) is used to wet the dressing to promote the absorption of blood into the dressing, thus preventing crusting on the wound edges.

C. Three weeks after two-layer plastic closure. Eversion and healing without crusting or tissue reaction.

D. Nine months following plastic closure. Flattening of scars without spreading.

FIGURE 11. A. One year following laceration closure elsewhere by ordinary interrupted sutures.

B. One year following excision and two-layer plastic closure with eversion of skin edges. Again, note absence of scar depression and spread.

FIGURE 12. "Dime store" nylon wrapped on intravenous tubing with No. 1844-5 Anchor brand needle tied on with three knots ready for use. Storz needle holder No. N-5700 with rounded edges and fine serrations which allow the instrument ties with minimal suture breakage. Fine skin hook should have short shank as shown. Ochsner diamond-jaw needle holder prevents twisting of the needle during insertion of subcuticular 5-0 monofilament nylon.

the incision improves the situation but the patient often complains of the length of the scar. Small triangular "darts" of skin can be excised with a No. 11 Bard-Parker blade to flatten these areas by removing the excess conical skin (figure 6).

Sutures

Except in the mucous membrane of oral and nasal cavities, catgut or silk should never be used on the face. These organic materials cause excessive foreign-body reactions with increased scar formation and, if buried, extrude through small pustules, leaving scars.

Permanent buried suture—For almost 20 years we have used twisted white nylon thread (dime store variety) for permanent sutures buried in the dermis. Lately, other white synthetic suture materials have become available. The strength of these synthetic sutures is superior to that of every suture except steel. When this suture material is buried at least 2 mm. beneath the epithelial surface, it rarely "spits," and when it does, it extrudes through a small pore with minimal scarring. It is only in mucosal closures that extrusion rules out its use. It rarely should be used in eyelids because these sutures can often be felt as little beads under the thin skin.

Temporary subcuticular suture—Temporary buried subcuticular sutures of 4-0 or 5-0 monofilament nylon are used to place a subcuticular running "drawstring" which is removed in two to three weeks.

Temporary surface suture—Temporary surface interrupted sutures of 4-0 to 6-0 monofilament nylon are tied with only the first half of a surgeon's knot and removed no later than 72 hours afterward. These merely correct any persisting unevenness or spreading of the wound following the closure with the two previous layers. Leaving these sutures in place longer than 72 hours will often cause crosshatching scars due to excessive tension or to small stitch abscesses.

Bandaging

A proper bandage should:

1. Protect the wound from contamination.
2. Prevent tension on wound margins.

3. Supply enough pressure, if necessary, to minimize postoperative bleeding.
4. Be kept as small as possible.
5. Restrict motion.

Dressings without pressure—For more simple closures requiring no pressure, Duke's Elastoplast No. 204 dressings suffice. Collodion bandages under slight tension can serve admirably in many cases. However, collodion should never be placed directly on a closure, as it can cause a chemical burn of subcutaneous tissue and also interpose an impregnable wall between the healing skin edges. Several narrow layers of gauze are applied over the closure, and fine-mesh gauze is then glued by its edges over this for protection. The wound can therefore "breathe," and maceration is avoided. Dressings should be changed only when necessary, i.e., for suture removal, loosening, inspection for hematoma, or undue swelling.

Pressure dressings—Where possibilities of hematoma or excessive swelling exist, moderate pressure dressings are employed. Rolled gauze over fluffed-up Kerlix can nearly always supply the necessary pressure and is the best in our hands. Elastic bandages should not be used, as large sloughs due to pressure necrosis can easily occur.

"Wet wick" dressing—Dihydrostreptomycin solution (1 gm. per 10 cc. normal saline solution) is used to moisten the dressing directly over the closure in all wounds. This tends to remove the blood between the skin edges before it clots, acting by capillary action as a lamp wick. If this clot is not removed, it can form an appreciable obstacle to accurate skin closure and lead to increased fibrosis. This is our standard form of dressing and is often combined with a pressure dressing above it.

Splints—Splints of plaster of Paris, wood, aluminum or plastic should be used wherever motion would normally occur and interfere with healing. The patient's habits, activity, etc. as well as the type and location of the wound should be evaluated when considering the type of dressing. The younger and more irresponsible the patient, the larger and more secure the bandage must be.

Conclusion

We have presented our modification of Halsted's subcuticular suture technic and a method of acquiring skill in its performance before the closure of human skin is attempted. We are firmly convinced from our experience that this technic is greatly superior to any other method of closure of facial wounds. It should be taught to all students of surgery prior to their independent operative experiences.

The routine use of silk and catgut in facial wounds is contraindicated. The continued use of large interrupted sutures in facial skin is not justified and should be condemned.

When Do You Refer a Child to a Psychiatrist?

HARRIS E. KAROWE*

Albany Medical College of Union University, Albany, New York

Introductory Comment

The role of the referring physician in psychiatric problems is a nebulous one. It is in essence more than a procedure, and, like the art of clinical intuition, is most difficult to teach. Through his own extraordinary maturity of viewpoint, Dr. Karowe has conveyed the role of the "social therapist" most effectively. Astute intelligence, experienced common sense, and a way of relating to patients are reflected here. Yet, the article has no scarcity of concrete rules for the guidance of good clinical judgment. This is, in addition, an unusually full and talented piece of writing—outstanding in every respect.—Franklin G. Ebaugh, M.D.†

DIFFICULT as it is to decide whether or not to have certain adult patients see a psychiatrist, the same problem can be even more perplexing with children. Superimposed on all the factors which confront us with a questionably disturbed adult is the consideration of constant flux in the growing and, therefore, always changing entity which is the child. There are so many factors which must enter into such a decision that to answer the title question well may prove impossible. However, it may be sufficient to establish certain general frames of reference whereby each patient may be assessed.

HARRIS E. KAROWE

Attitude Toward Referral

Referral to a psychiatrist still is, not only for the patient but also for many referring physicians, a more portentous step than referral to any other specialist. It is as though such referral, per se, constitutes a value judgment of the patient. The intensity with which we want to avoid the "unnecessary" referral to the psychiatrist is a reflection of how we think the patient's family regards a visit to the psychiatrist, and, in many cases, how we

*Director, Schenectady County Child Guidance Center, Schenectady; Assistant Clinical Professor of Psychiatry, Albany Medical College of Union University, Albany, New York.

†Editorial Consultant in Psychiatry, POSTGRADUATE MEDICINE; Emeritus Professor of Clinical Psychiatry, University of Colorado School of Medicine, Denver, Colorado.

ourselves regard psychiatry. In this respect we need but reflect on how much less hesitant we would be to send our own wife or child to the allergist than to the psychiatrist. Similarly, while we *tell* our patient to see the allergist, we often *ask* him if he will see the psychiatrist. In no other field of medicine is it considered so essential to refer only when absolutely unavoidable.

We all are aware that sometimes there still exists a stigma on those who see the psychiatrist. But we physicians must be in the vanguard in this respect and indicate that we recognize the need for help with psychiatric illness to be no less respectable than with any other illness. If we recognize this fact, then our own anxiety about consulting a psychiatrist regarding a patient will diminish, and we will no longer feel as though we are sending our patient "down the river" when we are only sending him down the street to our colleague. We must always remember that referring a patient to a psychiatrist is not discharging him. We may merely be getting an opinion on the patient; we send him for evaluation, not necessarily for treatment. To strive to limit referrals only to those patients in need of psychiatric treatment would reduce markedly the potential value of the psychiatrist to the nonpsychiatric practitioner. Just as the surgeon is best qualified to decide if an operation is indicated, so too should it be the psychiatrist who determines if psychotherapy is indicated.

Does it follow then that every child with any kind of emotional problem should be sent promptly to the psychiatrist? No, not at all. What is implicit thus far, though, is that the practitioner need not feel guilty if he does send someone to a psychiatrist and then learns that psychotherapy is not really required; he will not have done the patient a disservice. At the Schenectady County Child Guidance Center we have not yet had an inappropriate referral, although we have not taken into treatment all the patients physicians have referred. We think or, at any rate, we hope that we have helped the referring doctors even in those cases with dispositions other than therapy. The referring doctor has been apprised of our ideas on the nature of the patient's disturbance, the psychodynamics which enter into it, and the management of the problem either by the referring physician or by some other agency.

The Practitioner as Psychiatrist

The issue then is not whom can we avoid sending to the psychiatrist, whom can we spare this disservice, but rather how can we decide whether the problem is of such nature as to be likely to yield to our own ministrations. In part, the answer to this is related to the level of psychiatric sophistication of the referring physician, to the extent of his experience in dealing with children's emotional problems, and to the degree of personal interest and time at his disposal to spend with the child in question and with his parents. In a child guidance clinic, about 6 to 10 professional man-hours are spent in the average diagnostic workup. Treatment for those problems which prove to need psychotherapy is, of course, even more time-consuming. Thus, the doctor might regard a problem as within his scope and still refer the child to a psychiatrist, for dealing with the problem might require more time than he cares to or can devote to it, even though the disturbance is not of greater severity than he can cope with.

Significance of Symptoms

There are many problems the practitioner can handle himself, but the troublesome fact is that the same symptom can be relatively benign in one instance and in another be the signal of a severe illness. For example, a learning disability may signify various levels of disturbance:

Sam, an eight year old boy, impressed all who knew him as being of sufficient intelligence, yet he had barely managed to pass the first grade and was doing poorly this year too. A very pretty boy with a soft manner, he often was the recipient of angry and biting comments from the man in whose class he had been since entering grade school. The teacher, in discussion with the principal, was able to see that he had been inordinately annoyed

by what he saw as Sam's effeminacy; he always had found distasteful those men who did not appear strong and virile. Sam was transferred to another class and, within a few months, was doing better than average work.

Much more often a child with a learning disability resembles Billy. At the age of 12 Billy had never done passing work in school, although he had been promoted every year but one. Although his I.Q. was 123, which placed him in the superior range, he could read at only third grade level and had almost equal deficits in his other subjects. But his troubles were not confined to school. He had very few friends, for most children found him too bossy and not at all a good sport. At home he would often be stubborn, uncooperative, petulant, and sometimes even prone to explode in a tantrum. He had been enuretic all his life. His learning disability was only one manifestation of a pervasive personality disturbance involving difficulty in handling adequately any of his aggressive feelings.

It even happens sometimes that a learning disability is only part of an extremely profound disturbance in which the child's perception of the real situations around him is seriously impaired and in which his poor learning is but one aspect of his poor contact with the world outside himself. This sort of situation, while usually readily recognizable, sometimes may be overlooked, and one such instance came to our attention this year:

John, a 16 year old boy, had spent the last 10 years, ever since first grade, in special classes in an excellent school system, always learning poorly. We were consulted about him, and because of some question as to the adequacy of his reality perceptions, we arranged an interview to see him. He had been seen by a psychiatrist some years previously and had been judged to be mentally defective, which accorded with his having spent almost all his school years in a special class for the retarded. A few years ago he had been tested by a psychologist who had reported an I.Q. under 70, and he had even been sent to the state institution for mental defectives. However, he had remained in the institution for only a number of months before it was decided he did not properly belong there, and he was returned to the community. In our study of him we found that he was a sly and manipulative youngster, far too shrewd to be of less than normal intelligence and able on some psychologic tests to demonstrate at least average intellectual capacity, although he was virtually devoid of learned information. His thinking was unrealistic and governed to an unhealthy extent by his instinctual impulses, and it was on this basis, because he was essentially a psychotic youngster, that he had been unable to learn, even though his intellectual endowment was not at all defective.

Thus, we see that the same problem, wherein a child of normal or superior intelligence does not perform academically at a level anywhere near that to be expected from his intellectual endowment, would warrant psychiatric referral for such children as John or Billy but not for Sam.

Criteria for Evaluation

It often is difficult for the child psychiatrist himself to evaluate the seriousness of a specific situation. Not only does he then examine the child for a number of hours, but he also often enlists the aid of special tests administered by a highly trained clinical psychologist in an effort to assess better the child's deeper thoughts and fantasies. It would seem logical for the physician to note the psychiatrist's criteria for making a final judgment and to plan to apply these or similar criteria in evaluating a child and in then deciding whether to handle him or to recommend referral. But again we run into difficulty, for these criteria require for their application a thorough knowledge of the child's emotional workings—the sort of knowledge it is not fair to expect the practitioner to have without rather extended training in psychiatry. However, some of these criteria may be useful as general working principles in assessing individual cases.

Is conflict internalized or still external?—In any presenting problem, we should like to ascertain whether the difficulty is situational or intrapersonal, external or already internalized, whether part of the conflict is represented by some person outside the child or whether

both sides of the conflict are within the child himself. Let us look at a few examples of this criterion. All children have a couple of basic worries: that they will lose their parents' love and protection, and that they will be destroyed or mutilated. Nightmares may be a manifestation of an exacerbation of this second universal apprehension, i.e., that part of the body may be lost.

When Aaron was four and a half years old his parents hired a new housekeeper. A rather elderly spinster, she did her work well, but she was very perturbed by Aaron's handling of his genitals. She thought of this as wicked, and in desperation she began to tell Aaron she would "cut it off" if he did not stop. He did stop, but his nightmares started about this time. Within a week of the time his parents learned of the threats, put an end to them, and reassured Aaron that such threats never would be carried out, he again slept through the night uninterruptedly. No psychiatrist was involved in the correction of this sleep disturbance, which had been precipitated by an external stress.

Similarly, we may decide that no psychiatrist is necessary if nightmares occur following a tonsillectomy, an accident or a severe beating by an older boy. However, even in such cases, when the provocation for development of symptoms is clear, we would begin to worry if the nightmares persisted for many weeks. In that event, a psychiatric evaluation would be indicated.

Regressed behavior may be a reaction to a stress which involves the first of the aforementioned basic worries, that of losing parental love and affection.

At three and a half Tommy, who had been toilet-trained a year before, began to have occasional "accidents" during the day, to wet the bed about two nights each week, and to be cranky, whiny and unusually demanding. The family physician learned of this when Anne, his five month old sister, was brought to the office for a routine inoculation. The doctor's questions revealed that Tommy had started nursery school two months before. He advised that Tommy be withdrawn from nursery school, explaining to the parents that Tommy's regression to babyish behavior was an unspoken statement that Tommy did not want to be pushed into growing up so fast. He informed them that going to school meant, to Tommy, relinquishing his parents' love and protection so that it could be given to Anne instead. Within a month of his being taken out of school Tommy was his old self again. The following year he was able to go to nursery school without any difficulty.

Parenthetically, it should be mentioned that sometimes the existence of a precipitating event for the appearance of symptoms is not reassuring but rather a warning of trouble ahead. For example, enuresis occurring after an operation in a previously trained child is likely to be refractory and to require extensive psychotherapy. Such children usually consider the operation, whatever it may be, as a "castration," i.e., as a mutilation, and often, even after a long psychoanalysis, cling to the "fact" of their castration and, concomitantly, to their enuresis.

Is disturbance pervasive or still limited?—Another criterion is whether the disturbance is limited in its effect on the child's functioning or has spread to include many or most of his activities, whether it has interfered with the child's developmental process, whether the child has stopped growing up. For example, when the complaint is that the child simply does not get along well with his mother, we should like to know whether his interpersonal difficulties are restricted to the home or whether he has trouble with his parents, his teacher and his contemporaries, i.e., in all his interpersonal relations.

A few years ago Mary, age nine, was referred for evaluation with the suggestion that the real trouble was not with Mary but that her mother just could not be firm enough with her. However, an hour's talk with the parents revealed that, while this did seem to them to be the crux of the matter and while Mary's constant friction with her mother was what disturbed them most, this hardly represented the extent of the trouble. Mary also had had temper tantrums ever since her sister was born, was very self-depreciatory and considered herself quite worthless and inadequate, and was be-

coming increasingly compulsive in her habits. Considerable improvement was obtained with only a half year of psychotherapy involving Mary and her mother.

Another example of the application of this criterion is that an occasional nightmare may not have much significance, but if nightmares occur a few times a week for many weeks they are of more import. In this instance a careful history may reveal that the child also has other symptoms of anxiety, such as various daytime phobias and fear of physical injury, with reluctance to engage in contact sports and extreme reaction to a minor cut or bruise.

Is the complaint a normal maturational phenomenon?—Another important consideration is whether the expressed complaint is actually what would be expected as part of the normal process of growing up. For example, sleep disturbances of short duration are not abnormal at various developmental phases.

Some very young children will show disturbance of their sleep patterns when they are acquiring new abilities, the most usual of which is learning to walk. It is as though the acquisition of this capacity to move away from the mother generates anxiety which interferes with falling asleep or staying asleep. Also, there is nothing abnormal about a sleep disturbance in a child of two, for his unwillingness to go to sleep indicates his burgeoning interest in the people and the world around him and his wish not to give up this increasingly important aspect of his life. Between the ages of three and six, during the oedipal period, any normal child may show a sleep disturbance which results in one of his parents getting up after they have retired. This interruption of sleep is not abnormal and stems from the usual unconscious wish in a child of this age to have his parents less close to each other. It will be only transitory unless it is handled incorrectly by his parents, i.e., unless they help transform it into a neurotic disturbance either by being very punitive and threatening or by indulging his wish to part them and thereby being seductive with him.

Sibling rivalry is normal, even though unpleasant; the two year old who shows only love for his three month old sister is suspect. Phobias in the second or third year are quite normal, e.g., of the vacuum cleaner or of the drain in the bathtub. These arouse in the child the fear that he may be made to disappear like his feces in the toilet. Frequent touching of the genitals, even while observed by adults, is not abnormal in a three year old, but in the school-age child who does it in the view of adults, it shows anxiety rather than pleasure; a boy this old is probably reassuring himself that everything is intact, or confessing, or asking for punishment.

Some sorts of turmoil are more abnormal by their absence than by their presence. The normal adolescent seems abnormal; he is a trial to his parents and teachers; he is predictable only in his unpredictability. We have little cause for worry with an adolescent provided his periods of misbehavior fluctuate with periods of really good behavior, his sadness with great happiness, his asceticism with self-indulgence, his selfishness with generosity, his egotism with humility, and his philosophizing with practicality. It is those adolescents who have given up, or never even entered into, the struggle with their instinctual impulses and the struggle to establish their independence, and who therefore present a constant, unchanging front to the world—even though it seems to be a good and compliant front—about whom we should worry.

It is thus very important to keep in mind that certain problem behavior has different significance at different times in a child's life. This is not a strange concept at all, of course, for we apply it to strictly medical problems without giving it a second thought. For example, we are not concerned if jaundice develops in a newborn infant on the third day of life, but we are very concerned if he becomes jaundiced when he is only three hours old. We consider anemia pathologic at five years of age but hardly so at five months. We are prepared for a drop in food intake at two years and, whether this is a purely physiologic phenomenon or also has psychologic causes, we do not become alarmed nor do we let his parents get alarmed. But if

a child radically decreases his food intake at four months or four years, then we do think something may be amiss and we look further. So we must always include in our thinking the concept of maturational level, of the normal maturational crisis which the infant, child or adolescent may be solving, and we must recognize that this normal process may produce symptoms, be they physiologic jaundice or a mild form of childhood sleep disturbance, puberal acne or the upsetting inconsistency of the adolescent.

Nature of the Symptom

There are other considerations too, such as the duration, constancy and intensity of the symptoms, and the nature of the particular symptom. For example, a symptom that has been present for a week is more likely to be relievable without psychiatric intervention than one that has been present for a year. This, of course, points up the prophylactic role the practitioner can play, for he sees a child much sooner after trouble starts than does the psychiatrist, and, provided he does not simply dismiss the problem with, "He'll grow out of it," but instead attempts to understand its genesis, either in a normal maturational crisis or in some disturbed interpersonal relationship, he can do much to prevent its evolving into a more serious disturbance.

Petty stealing is an occasional event in the lives of most children; of different import is compulsive stealing, which warrants psychiatric evaluation. Most children have phobias of various sorts at various ages, but when certain phobias persist without change over many months and are of such intensity as to interfere with the child's or the parents' enjoyment of life, referral to a psychiatrist is in order. Most children do some lying at an early age to make tolerable by denial and fantasy the frustrations of their daily lives, and at a later age to avoid punishment or to gain certain material ends. If the lying persists unabated, even after the reasons for fear of punishment and for acquisition of material things are discussed with the child, he should be referred for psychiatric evaluation. Also, certain symptoms are more ominous than others. To mention only a few, a tic almost always warrants psychiatric study, as does stuttering, repeated soiling in a school-age child, fire setting, or running away from an ostensibly good home.

An illness which is regarded as a psychiatric emergency but which, nevertheless, often can be handled by the practitioner is the school phobia. If handled early, and preferably in its incipient stage, it can be prevented from developing by the doctor's intervening with firmness and assurance. He should tell the parents, without any uncertainty, that the child must go to school; he should tell the child he must go and, if he has a good relationship with him, he can stress that he wants him to go for his sake. The doctor should explore with the school administration the possibility of the mother's staying in the classroom with the child for gradually diminishing lengths of time, or the child's staying in the office if he finds the classroom too much for him. Serving as mediator and integrator in this way, and using these or other comparable devices, the practitioner can get the child back to school and thus avert serious illness. However, because it becomes increasingly difficult to get the school-phobic patient back the longer he has been out of school, the practitioner should make a referral to the psychiatrist if improvement does not occur within a week.

Although the infant is not at the time obviously affected by emotional disturbance, it is advisable to refer a mother to a psychiatrist if the practitioner finds that she is even moderately depressed for more than a few weeks after delivery. We see many children who show serious emotional disturbance, and even pseudo mental retardation, in whom the difficulty is traceable to a significant maternal postpartum depression which resulted in the child's being deprived of the attention and affection which the healthy mother gives to her infant.

Do the Parents Need Education or Treatment?

In many instances the parents will subtly sabotage the doctor's efforts to help the child:

Sandra, who had a severe, long-standing school phobia, finally had reached the point in treatment where she could tolerate going to school. In the second week of this improvement her mother kept her home because, she said, Sandra seemed to be catching cold. This solicitousness became especially suspect when we learned that Sandra's sister also had seemed to be catching cold but had been allowed to go to school. The mother based this decision on the sister's having an arithmetic test that day, although the mother knew how very important it was that Sandra go to school regularly. Earlier in treatment, when the mother already knew that Sandra's real fear was not of going to school but rather of the terrible things she thought might happen to her mother while she was away from home, the mother had been wont to threaten Sandra when exasperated with her. Interestingly, her threats would be that she would commit suicide or that she would pack her bags and leave the family. Thus, she fed her daughter's fears, saying in effect that it indeed was possible for Sandra to lose her mother.

This is an example of the fact that parents fall into two major categories, those who need to be educated and those who are acting out their own neurotic problems. In general, the nonpsychiatrist can deal with the parents and children who merely need education, e.g., with the adolescent's parent who, in spite of his own better judgment, has been so convinced by what he thinks he has read that he sets no limits by which his adolescent son can be guided. The physician can enlighten him on the value of a parent's establishing clearly for an adolescent, no matter how independent the boy may seem to want to be, that certain types of behavior are definitely expected and certain others definitely not to be tolerated. On the other hand, reasoning with a parent who is driven by unconscious neurotic forces will be unavailing, and the child of such a parent almost always requires referral to the psychiatrist.

Parental Motivation

In this context we should mention the factor of parental motivation, especially with regard to the potential efficacy of psychotherapy but even with regard to the level of productiveness of a diagnostic evaluation. At one extreme is the parent who asks to be referred to the child psychiatrist; such request always should be granted. As has been said by an authority, a woman who asks to see a psychiatrist should have her head examined. But at the other extreme is the parent who is not at all distressed by the child's symptoms and behavior, or who does not even recognize the existence of any problem with the child. Where the motivation to seek help is so slight, where the parents are not really in accord with a referral, where they come to the psychiatrist only because they are told to do so, psychotherapy will most likely be ineffective, and even the diagnostic study may fail to elicit the information necessary for a clear formulation of the genesis, nature and severity of the child's difficulty. With such parents it is very valuable to spend much time in an effort to help them realize that a problem may exist, so that they may approach the psychiatric evaluation in a more positive frame of mind.

To Refer Is Conservative

Somewhere we should say, and perhaps this is as good a time as any, that having a patient enter psychiatric treatment is by no means an assurance that his troubles are over; there are those who would say they have just begun! It is sad but true that a certain percentage of persons do not improve despite good psychiatric attention. The psychiatrist's contention is that he could have accomplished more if he had seen the patient earlier, before the problems had burrowed so deeply into the child's personality structure and become so ingrained in his character. This, too, constitutes an argument for not sitting too long on emotional problems in the hope they will improve spontaneously. The earlier something is done about them, either by the practitioner or by the psychiatrist, the better. It is not too unlike the attitude we learned long ago with regard to operation when faced with a possible appendicitis: "When in doubt, take it out." With emotional problems, too, doing nothing may not be the conservative course.

Normal Versus Abnormal

Always, however, we come back to the unavoidable issue of determining where the line is to be drawn in the spectrum that extends from clearly normal to clearly abnormal. To this question no good answer can be given. It requires an extended experience in handling emotional problems, in seeing how to apply criteria like those previously mentioned, in correlating one's own evaluations of situations with those of the child psychiatrist and learning from those instances where the correlation may be low, and in gaining more and more knowledge of the deeper processes of feeling and thinking in children. When it becomes possible to know why a child presents a certain picture, it is comparatively easy to decide what to do about it. Without knowing the "why," we are left essentially in the position of symptomatic management, a position, unfortunately, of less than rational medical practice. Consequently, it appears that, in many if not most instances, management of a problem is likely to be facilitated by psychiatric evaluation of the child and his family, so that the practitioner may have some further idea of the personality structure, interactions, and conflicts not only of the child but also of the rest of the family. From such repeated collaborations, the practitioner can acquire some of the special insights that psychiatry has gained, and be in an ever stronger position himself to handle the emotional problems which come to his attention.

Summary

Some observations have been made on attitudes toward psychiatric referral and on how they may serve as deterrents. Using a learning disability as an example, it has been shown that the same complaint may have different significance in different contexts. Certain criteria for evaluating the portent and management of a disturbance have been discussed. Among these are whether the difficulty is situational or internalized, whether the disturbance is pervasive or limited, whether it is a part of a maturational crisis, whether it has been unchanging and of long duration, whether the parents are creating and maintaining the problem because of their own neurotic conflicts, and whether the parents are motivated to attain an alteration of the family's dysfunction. A number of symptoms, some of which are persistent sleep disturbance, compulsive stealing, stuttering, fire setting and repeated soiling, have been mentioned as sufficient indication in themselves for psychiatric evaluation. The role of psychiatric attention to a mother in a postpartum depression has been pointed out as a means of avoiding possibly serious interference with the child's development. The value of collaboration between psychiatrist and practitioner has been briefly discussed.

Postgraduate Clinical NOTES

155. THE BRAIN

The individual human brain and mind is the most complicated and highly organized piece of machinery that has ever existed on this earth. So-called electronic brains can perform extraordinary tasks with superhuman rapidity, but they have to be given their instructions by men. The human organism can give instructions to itself, and can perform tasks outside the range of any inanimate machine. Though at the outset it is a feeble instrument equipped with conflicting tendencies, it can in the course of its development achieve a high degree of integration and performance.

Julian Huxley, The future of man, *Bulletin of the Atomic Scientists*, December 1959, pp. 402-405

The Influence of Chronic Undernutrition on Bone Growth in Children

SAMUEL DREIZEN,* ROBERT E. STONE† AND TOM D. SPIES‡

Northwestern University Medical School, Chicago

GROWTH is a cardinal characteristic of the living organism. It is manifested physically by size, shape and proportion, and it stems from the simultaneous increase in cell mass, number and complexity. Control rests in the continuous interplay of genetic and environmental forces operating through the endocrine and nervous systems on the end organs. Harmony among these forces results in orderly growth progress; disharmony may lead to bizarre growth disturbances.

No other end organ is as technically amenable to measurement throughout the growth period as the skeletal system. Calcium salts in roentgenographically detectable quantities begin to be deposited in the skeleton during the latter part of the fetal period and increase progressively until the cessation of skeletal growth. In the embryonal and fetal stages, bone arises by differentiation of mesenchymal cells into osteoblasts. In the postnatal period, growth and reconstruction of bone occur by the osteogenic activity of reticular, endosteal and periosteal cells which are transformed into osteoblasts during bone formation.

Bone is assumed to contain enzymes common to a wide variety of cells. There is no conclusive evidence, however, that any particular enzyme system is required for the calcification of the matrix of bone as distinguished from the matrix of cartilage. Phosphatase may play an important role in preparing the cartilage matrix for calcification, but once the property of calcifiability has been established, the presence of phosphatase is no longer necessary. Enzymes may take part in the resorption of bone during remodeling, since mineral and matrix are dissolved simultaneously. Resorption, which is mediated mainly but not exclusively by the osteoclasts, always progresses inward from the surface and never arises in the deeper layers. The process of bone resorption, an integral phase of skeletal development, apparently involves

*Associate Professor, Nutrition and Metabolism; †Professor, Nutrition and Metabolism; ‡Late Professor, Nutrition and Metabolism, Northwestern University Medical School, Chicago, Illinois.

Northwestern University studies in nutrition at the Jefferson-Hillman University Hospital, Birmingham, Alabama. From the Department of Nutrition and Metabolism, Northwestern University Medical School. These studies were supported by grants from Swift and Company, Carnation Company and Gerber Products Company.

SAMUEL DREIZEN

ROBERT E. STONE

the concurrent depolymerization of mucopolysaccharides, digestion of collagen, and chelation of bone salts.

Bone tissue has a very low metabolic rate and is in a continuous state of flux throughout life. The osteocytes have a limited life span and cannot regenerate, since they do not undergo mitotic division. Old bone and old osteocytes are removed and replaced by new bone and young osteocytes. Thus, ossification and resorption are more or less continuous processes which depend on the maintenance of the normal homeostatic mechanisms which regulate bone metabolism.

Disharmony between ossification and resorption may result in disturbances in the development of the skeleton as seen in osteogenesis imperfecta and osteopetrosis. In osteogenesis imperfecta (figure 1), the defect is in the osteoblasts which are retarded in form and in differentiation. The bone is formed slowly and in deficient amounts. Osteoclastic activity is usually unaffected. In osteopetrosis (figure 2), bone deposition proceeds normally but resorption is restricted consequent to a reduction in osteoclastic activity. The long bones become sclerotic and clubbed at the ends, and have very narrow marrow cavities. Such changes represent a failure of bone resorption to keep pace with bone formation.

In children, the formation of new osseous tissue at the growing ends of the long bones is normally an orderly and efficient process. The progression of events in bone production at the cartilage plate between the epiphyseal and diaphyseal bone sites begins with the growth of new cartilage from germinal cells just under the ossification center. The cells nearest the metaphyses undergo senescence and degeneration with precipitation of lime salts in their matrix. Subsequently the calcified cartilage is eroded into a honeycomb of cell spaces by capillary tufts and osteoclasts advancing from the bone marrow. Most of the calcified cartilage is incorporated directly into the subjacent bone trabeculae by osteoblasts; the remainder is resorbed by osteoclastic activity. The submetaphysis and cortex undergo continuous revision and remodeling. As the bone enlarges, some of the trabeculae formerly in stress-bearing alignment are resorbed by osteoclastic activity and replaced by hematopoietic marrow. New trabeculae are formed to meet new stresses. The cortex is excavated internally and augmented externally by periosteal osteoblasts. The aggregate of the entire process is continuous bone growth.

Specific nutritional deficiency states with a profound effect on the development of the long bones in children are scurvy and rickets. In scurvy (figure 3), the earliest skeletal change is an enlargement of the diaphyseal ends. Trabeculae on the diaphyseal side of the epiphyseal line undergo fragmentation. Diffuse absorption of calcium salts gives the bone end a translucent ground-glass appearance. A broadened band of temporary calcification forms above the epiphyseal plate. On the diaphyseal side a radiolucent line is formed by the inhibition of osteoblastic development and matrix formation. The line is homogeneous and runs across the end of the bone, creating the appearance of a double epiphyseal line. The ossification center develops a ring of calcification at the edge, giving the impression of an ossification center within an ossification center. As the disease progresses, subperiosteal hemorrhages develop primarily in the region of the epiphyseal plate where the periosteum is firmly attached. Subsequently, spicules of periosteal new bone form along the detached periosteum and project perpendicularly from the region of the epiphyseal line. Eventually the periosteum may be stripped off from the entire shaft. Extensive subperiosteal hemorrhages and superimposed trauma may produce epiphyseal separation, usually in the proximal epiphysis

FIGURE 1. Effect of osteogenesis imperfecta on developing skeleton of the hand and forearm. Chronologic age 11 years three months; skeletal age 11 years two months.

of the humerus and distal epiphyses of the femur and tibia.

The characteristic scorbutic histopathologic changes at the epidiaphyseal junctions of the long bones are indicative of a decreased growth rate and a qualitative defect in formed cartilage and bone. Newly formed cartilage is deficient in collagen. Compact bone is often replaced by spongiosa. In acute or advanced scurvy, growth of the long bones may cease altogether.

In rickets the formation of the organic matrix of bone by osteoblasts is undisturbed. Mineralization of the matrix is impeded and osteoid tissue is produced instead of bone. Long bones grow in thickness at a normal rate. The diaphyseal ends undergo enlargement, fraying and cupping (figure 4). The zone of osteoid formation between epiphysis and diaphysis is widened. Osteoporosis is generalized. Shafts of the weight-bearing long bones undergo bowing with cortical thickening on the concave side and thinning on the convex side. Spontaneous fractures may occur but the cortex is never broken through except by trauma. Endochondral ossification

FIGURE 2. Effect of osteopetrosis on developing skeleton of the hand. Chronologic age 35 months; skeletal age 33 months.

is retarded and often ceases temporarily in rickets.

The framework of growing bone hardens immediately after it is formed. The initial response of young bone to growth-disturbing factors is difficult to reverse unless corrective action is taken within a fairly short time. Routine roentgenographic study of the form, density, speed of growth and anomalies of young bone is diagnostically helpful in gauging the effect of systemic disturbances which influence bone growth in a particular child. The first reaction of young bone to growth-impeding factors is always localized in and around the cells of the vegetative growth cartilage. When the physiologic disturbances are prolonged, the new parts of the cortex are protected temporarily by the growth cartilage and subperiosteal tissue. Eventually the growth cartilage reacts as a unit. The number of cartilage cells is reduced and new bone

FIGURE 3. Bone changes in scurvy.

FIGURE 4. Bone changes in rickets.

production is limited in speed and extent.

The regulators operative at the site of ossification are located in the growing bone edge and in the bone marrow. There is no interstitial formation of new bone in the cortex. The regulators are probably morphologic determinators, since the trabeculae are the least reversible part of labile young bone. The regulators of ossification continue functioning for a relatively long time even under the strain of protracted undernutrition. When ossification is ultimately affected, the vitality of the growth cartilage is the first to weaken. New trabeculae formed under such conditions are stunted and develop in caricature, ossification continuing in the warped and limited matrix.

An irreversible reaction characterized by distortion of the whole bone has rarely been seen in young undernourished children in the Nutrition Clinic of the Jefferson-Hillman University Hospital, Birmingham. Nor does whole bone distortion take place later than usual in these children, although they are small and slender and tend to grow slowly during early childhood. Studies on over 2000 children at the Nutrition Clinic during the past 20 years indicate, however, that continuous undernutrition during infancy, childhood and adolescence affects the growth and maturation of the skeleton to a detectable degree. Specifically, the skeletal stigmas associated with growth and nutritive failure in the children of the Nutrition Clinic series include:

1. A failure to attain expected stature—Comparison of the height and weight of 561 children with chronic nutritive failure with a group of adequately nourished, ethnically comparable children from the same geographic area showed a substantial lag in height and weight to be present by the third year of age.[1] Thereafter, the weight lag increased progressively in both boys and girls. In the undernourished boys the height lag became increasingly greater after three years of age, whereas

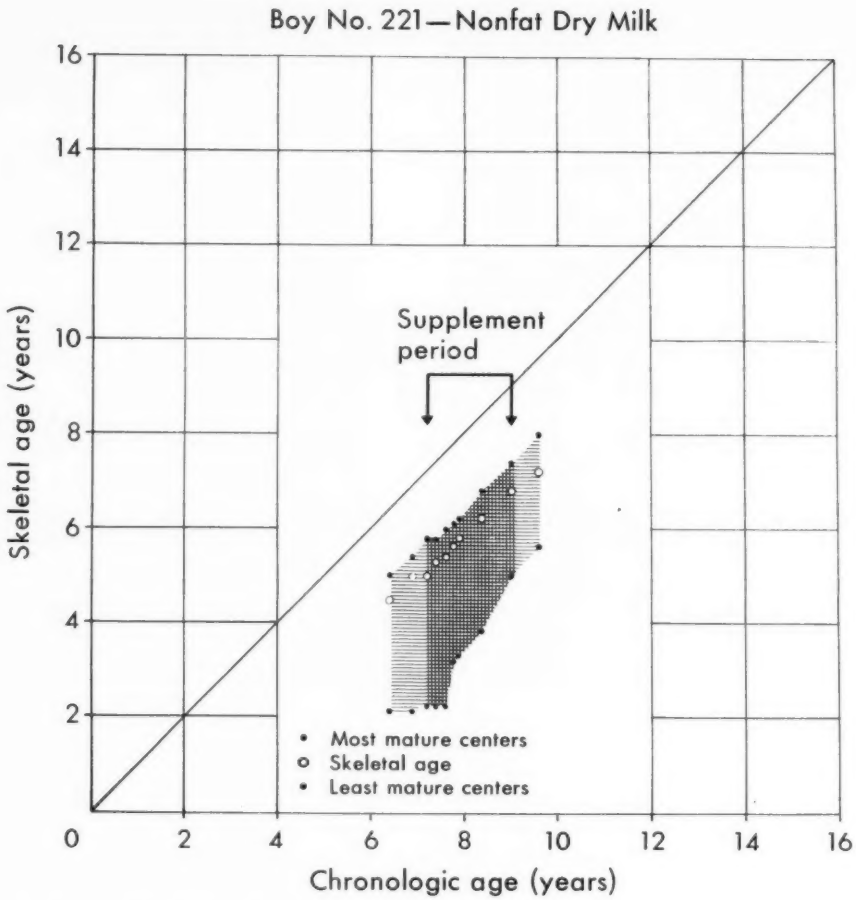


FIGURE 5. Graph showing that asymmetry in bone development in children with nutritive failure appears very early in course of skeletal maturation.

that in the girls remained fairly constant. By the sixteenth year of age, the mean differences between the groups with and without nutritive failure were 20.62 lb. and 2.68 in. in the boys and 13.50 lb. and 1.55 in. in the girls.

2. *A high degree of asymmetry in the maturation of the hand skeleton*—Assessment of skeletal maturity by the Todd inspectional method involves the timing of the successive irreversible stages which specifically characterize the postnatal development of each articular surface and epiphyseal cartilage plate. In standards constructed for use with the Todd technic, bone age determined from the maturational progress of each ossification center in the hand and wrist is conventionally equated in a 1:1 ratio. Theoretically, each ossification center should mature at the same rate; actually, complete symmetry in bone development is exceedingly rare. The bones of the hand and wrist are an aggregate of partially independent elements despite a tendency to act somewhat as a unit in development.

Quantitatively, the degree of skeletal asymmetry throughout the growth period can be expressed by the Red Graph method.[2] In this procedure, the stage of development of each ossification center is identified in serial roent-

genograms. The values ascribed to the most advanced and least advanced bones are plotted to delimit a zone which includes the maturities of all the other centers in the skeletal area. Asymmetry in bone development in children with nutritive failure appears very early in the course of skeletal maturation (figure 5). The degree of variability in maturation of the ossification centers in the hand skeleton of 740 children in the growth study group at the Nutrition Clinic was determined from assessments of single roentgenograms selected at random from the series available for each subject. For 371 boys, the mean difference between the most advanced and least advanced ossification centers was 24.9 months, and for the 369 girls, 19.1 months.[3]

3. A slow rate of skeletal maturation—The degree to which chronic undernutrition retards skeletal maturation was measured from skeletal age determinations derived from assessments of serial roentgenograms of 740 children.[3] The arithmetic mean of the ages assigned to each bone constituted the skeletal age. In 371 boys, the mean amount of retardation in skeletal age was seven months at three years of age, 12 months at 12 years of age, and 24 months at 18 years of age. The corresponding deficits for 369 girls were nine months at three years of age, 15 months at 12 years of age, and 22 months at 18 years of age. In contrast, in 53 boys and 80 girls without nutritive failure, the mean lag in skeletal age at 18 years of age was only 0.49 month and 0.63 month, respectively.[4]

4. A considerable frequency and variety of anomalies in the bones of the hand skeleton—The relative frequency of bone anomalies was determined from examination of roentgenograms of the left hand and wrist of 266 children ranging in age from 5 to 14 years.[5] The subjects were grouped on the basis of skeletal maturation and nutritional status. The mean number of epiphyseal anomalies (supernumerary epiphyses, pseudoepiphyses and hiatuses in the bone shafts) in 142 children with nutritive failure was 1.94; in 124 children without nutritive failure, it was 1.23. In 200 with retarded skeletal age, the mean number of epiphyseal anomalies was 1.84 in contrast to 0.91 in 66 children with no skeletal age retardation. The incidence of epiphyseal anomalies was significantly greater in children with nutritive failure than in children without nutritive failure regardless of the rate of skeletal maturation. Conversely, the incidence of epiphyseal anomalies in children with a lagging skeletal age was significantly greater than in those without a skeletal age lag regardless of nutritional status. No significant difference was noted in the frequency of nonepiphyseal anomalies between the groups differentiated on the basis of nutritional status and rate of skeletal maturation.

5. A noteworthy persistence of radiopaque transverse lines in the distal end of the shaft of the radius—The distalmost 10 mm. of full-length roentgenograms of the radial shaft of 235 children grouped on the basis of nutritional status and rate of skeletal maturation was inspected for complete and incomplete transverse lines of interrupted bone growth (figure 6).[6] Only four of the 235 children were free of both bone scars and remnants in the area investigated. A similar incidence in number of children affected and in the mean number of scars per child was found in the groups with and without nutritive failure and in those with fast and slow rates of skeletal maturation. Resorption of bone scars was related, however, to nutritional status. The group with nutritive failure had a statistically significant higher number of scars and lower number of remnants than the group without nutritive failure. Irrespective of nutritional status and rate of skeletal maturation, the incidence of scarring was significantly lower in children above 11 years of age than in those below this age. Thus, while nutritional status did not appear to play a role in susceptibility to bone scar formation, it did appear to influence the rapidity with which children recovered from the metabolic disturbances productive of bone scars. Specifically, the group without nutritive failure averaged 47 per cent more incomplete scars and 59 per cent less complete scars than did the group with nutritive failure.

Fine transverse lines of increased density were seen to appear in the roentgenograms of

FIGURE 6. Multiple bone scars in boy with nutritive failure and recurrent tonsillitis.

a. Chronologic age 10 years nine months.
b. Chronologic age 11 years six months.
c. Chronologic age 11 years nine months.
d. Chronologic age 12 years one month.
e. Chronologic age 12 years nine months.

the radius of some children with severe nutritional deficiencies after their diet was supplemented with reconstituted dry milk. The growth of these children was retarded when they first came under observation and their bones were poorly mineralized. Following the addition of milk to their diet, mineral and other osseous material probably began to be deposited in greater concentration than before. This presumably occurred before the rate of bone growth had increased correspondingly; consequently, an area of bone of increased density visible on the films as a thin transverse line was produced. When an equilibrium was subsequently established between the rate of bone growth and the accelerated rate at which mineral and other substances were being deposited, the new bone, while somewhat denser than that laid down before the dietary supplement was instituted, became normally homogeneous. The transverse line remained for a time as a scar to mark the point at which the augmented rate of ossification began.

6. A delayed fusion of the epiphyses in the hand and wrist—The gross roentgenographic manifestations of the successive stages of bony union between shaft and epiphysis were converted into an arbitrarily devised scale of epiphyseal closure. This scale was used to evaluate the fusion status in 21 bones of the hand and wrist of 251 ethnically comparable adolescents 16 through 18 years of age.[4] Compari-

FIGURE 7. Retarding effect of nutritive failure on epiphyseal fusion in skeleton of the hand.
a. 18 year old boy with nutritive failure.
b. 18 year old boy without nutritive failure.

sons were made between subjects grouped on the basis of nutritional status and over-all body size. In the group with nutritive failure there was a delay in epiphyseal fusion which averaged slightly more than one year in each sex as compared to the group without nutritive failure (figure 7). The delay in fusion was quantitatively similar in boys and girls despite the more rapid rate of skeletal maturation characteristic of girls. In the absence of primary hormonal disease, delay in epiphyseal fusion was not related to over-all body size.

7. *A retarding effect on the appearance of the postnatal ossification centers in the hand and wrist*—Comparison of the roentgenographically detectable advent of ossification in 31 centers of the hand and wrist of 301 undernourished boys and 240 undernourished girls with the age standards for the appropriate sex showed that the mean time of appearance of each of the centers was delayed in each sex (figure 8).[7] The mean amount of delay in the boys exceeded that in the girls for all but three centers. The frequency of retardation in onset of ossification surpassed the combined frequency of centers appearing either early or on schedule to a statistically significant degree for 29 and 26 of the 31 centers in the boys and girls, respectively. Some or all of the assessable centers were delayed in 504 (91.3 per cent) of the 541 children. The delay in advent of ossification was much more pronounced in the carpals than in the metacarpal and phalangeal epiphyses. Quantitatively, in the boys the average delay ranged from 1.2 months for the adductor sesamoid of the thumb to 28.9 months for the greater multangular; in the girls it was

FIGURE 8. Retarding effect of nutritive failure on appearance of postnatal ossification centers in developing skeleton of the hand.

a. Age seven years six months, before milk supplementation.

b. Age nine years, after milk supplementation.

from 1.8 months for the proximal phalanx of the third digit to 18.3 months for the greater multangular.

8. A specific seasonal distribution in the appearance of the postnatal ossification centers of the hand and wrist—The time of appearance of 31 postnatal ossification centers was determined in roentgenograms of the hand and wrist of 282 undernourished children.[8] The onset of ossification in these centers followed a seasonal pattern which was not related to sex, type of center, or month of birth. The number of centers presenting in the summer was greater than that emerging in any other season to a statistically significant degree. The temporal coincidence of a peak in occurrence of new ossification centers and of a diminution in rate of general body growth appeared to be related to a seasonal variation in the availability and utilization of specific nutrients and accessory food factors.

9. Fields of extensive demineralization in the bones of the hand and wrist—Bone quality as an indicator of the vicissitudes of health is reflected in the amount of coarseness or fineness of the trabeculae comprising the spongiosa; by the presence or absence of breaks in the spongiosa which, if present, appear as areas of increased radiolucency; by textural compactness and thickness of the cortex; and by the degree of mineralization of spongiosa and cortex as shown by the intensity of radiopacity (figure 9). Examination of bone quality in a group of 82 undernourished children showed that the thickness of the cortical bone using the metacarpals as the location of analysis was submedium in 42 per cent; the amount of spongiosa was subnormal in 62 per cent, and it frequently had a cindery appearance.[9] Patches of increased radiolucency were noted in 68 per cent, and the quality of the compact cortical bone was below average in 100 per cent. Limited and local improvement in bone quality occurred when milk was given as a dietary supplement. The most prominent change was reduction in number and extent of the radiolucent areas.

10. Age variation in response of retarded

FIGURE 9. Improvement in mineralization of developing skeleton of the hand by milk supplementation in child with nutritive failure.

a. Before milk supplementation.

b. After milk supplementation.

skeletal maturation to dietary supplements—The human growth-promoting properties of nonfat dry milk were compared in undernourished preadolescents and adolescents.[10] Both of the groups had evidence of substantial retardation in skeletal maturation attributable to dietary inadequacies. The supplement* was given six days per week for six months and was equivalent in nutrient value to 2 qt. of skim milk per day. The milk supplement promoted a statistically significant increase in both size and skeletal maturation in the preadolescent group. The adolescent group underwent a significant acceleration in rate of general body growth without a concurrent discernible increase in rate of skeletal maturation. The bone response was confined almost exclusively to size, with maturation being relatively unaffected. The lack of a measurable increase in rate of skeletal maturation in the adolescent group during the period of supplementation accords with Todd's observation that if inhibition in progress of skeletal maturation during the preschool period is sufficiently great as to be apparent, the chances of restoration during adolescence are very slight.

In young undernourished children the skeletal and somatic growth response to an adequate dietary supplement is demonstrable only as long as the supplement is continued. As shown in figure 10, withdrawal is followed by relapse, reinstitution by remission. These data were derived from 10 undernourished children with retarded skeletal and somatic growth who were given dietary supplements of reconstituted nonfat dry milk equivalent in nutrient value to 2 qt. per day, six days per week, for six months on two separate occasions. The mean growth rates increased significantly during the two periods of supplementation and dropped sharply each time the dietary addition was discontinued.

11. Disproportionate maxillary and mandibular growth—The entire face grows downward and forward with a fairly constant relationship to the anterior cranial base. The mechanism of mandibular growth is basically different from that of the maxillary part of the face. In the maxilla, growth is primarily sutural and initiated by proliferation of con-

*Carnation instant nonfat milk.

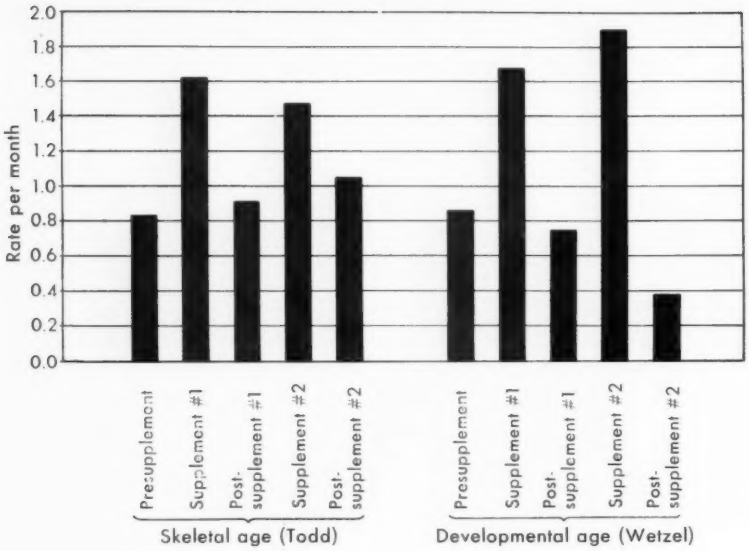


FIGURE 10. Response of retarded skeletal and somatic growth in 10 children during two periods of nonfat dry milk supplementation.

nective tissue at the suture lines. In the mandible, the main growth center is the hyaline cartilage of the condyle. Condylar growth increases the over-all length of the mandible and height of the ramus. Appositional growth contributes to the increase in the over-all size of both jaws. Mandibular growth is considerably more rapid than maxillary growth and apparently more sensitive to growth disturbances. Cephalometric studies of 88 children with chronic undernutrition at the Nutrition Clinic showed they had a generalized tendency to a more backward divergent face that was attributable to greater growth retardation in the mandible than in the maxilla.[11] The discrepancies in jaw relationship diminished with increasing age, the diminution being greater in children whose dietary deficiencies were corrected with milk supplements than in those who did not receive the added milk.

The foregoing manifestations demonstrate that adverse nutritional influences act on the skeleton during the growth period to alter physiologic and maturational progress. With the attainment of skeletal maturity, the active biochemical changes constantly evident in the skeleton at all ages are reflected in the equally changing internal structure to a degree often detectable roentgenographically. The extent of fluctuation in mineralization during pregnancy and lactation in a young mother delivered of a full-term infant at 19 years eight months of age while on a marginal diet is shown in figure 11. The films were taken one year before delivery and four and 12 months post partum. The mother gained 13 lb. during the pregnancy and did not take any calcium supplements during this period. The infant weighed 8 lb. 4 oz. at birth and was breast-fed for eight months. The roentgenogram taken four months post partum during lactation shows a loss of the labile mineral in the interstices between the trabeculae of the spongiosa. The loss is most marked in the carpals, metacarpal heads and distal end of the radius. Within the trabeculae the changes are manifested as modifications in thickness and occasional fragmentation. The film made four months after weaning (one year post partum) shows some improvement in mineralization, but it is still considerably below the prepregnancy level.

The conclusions to be derived from these studies are inevitable. No cell in the body is beyond the pale of nutrition and metabolism. None is immune to inanition. Periods of prolonged nutritional deprivation affect developing bone to a roentgenologically recognizable

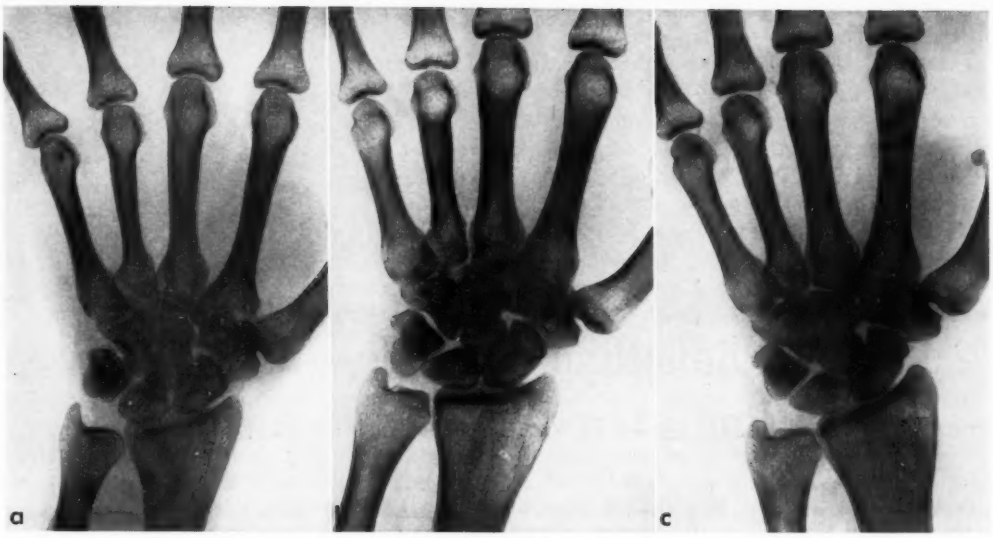


FIGURE 11. Effect of pregnancy and lactation on the mineralization of skeleton of the hand in a young mother on a marginal diet.

a. Chronologic age 18 years eight months (three months before pregnancy).

b. Chronologic age 20 years (four months post partum).

c. Chronologic age 20 years eight months (four months post weaning).

degree. During such periods, intracellular activity is slowed or suspended, growth ceases, size is diminished, and shape is altered. No cell, regardless of location, can suspend animation indefinitely without undergoing irreversible changes. For successful treatment of nutritive and growth failure, it is imperative that proper and persistent therapy begins before damage becomes irremediable.

REFERENCES

1. DREIZEN, S., CURRIE, C., GILLEY, E. J. and SPIES, T. D.: The effect of nutritive failure on the growth patterns of white children in Alabama. Child Development 24:189, 1953.
2. PYLE, S. I., MANN, A. W., DREIZEN, S., KELLY, H. J., MACY, I. G. and SPIES, T. D.: A substitute for skeletal age (Todd) for clinical use: The Red Graph method. J. Pediat. 32:125, 1948.
3. DREIZEN, S., SNODGRASSE, R. M., WEBB-PEPLOE, H., DREIZEN, J. G. and SPIES, T. D.: The sites of maturational strength and weakness in the developing hand skeleton. Am. J. Roentgenol. 82:490, 1959.
4. DREIZEN, S., SNODGRASSE, R. M., WEBB-PEPLOE, H. and SPIES, T. D.: The effect of prolonged nutritive failure on epiphyseal fusion in the human hand skeleton. Am. J. Roentgenol. 78:461, 1957.
5. SNODGRASSE, R. M., DREIZEN, S., CURRIE, C., PARKER, G. S. and SPIES, T. D.: The association between anomalous ossification centers in the hand skeleton, nutritional status, and rate of skeletal maturation in children five to fourteen years of age. Am. J. Roentgenol. 74:1037, 1955.
6. DREIZEN, S., CURRIE, C., GILLEY, E. J. and SPIES, T. D.: Observations on the association between nutritive failure, skeletal maturation rate and radiopaque transverse lines in the distal end of the radius in children. Am. J. Roentgenol. 76:482, 1956.
7. DREIZEN, S., SNODGRASSE, R. M., WEBB-PEPLOE, H. and SPIES, T. D.: The retarding effect of protracted undernutrition on the appearance of postnatal ossification centers in the hand and wrist. Human Biol. 30:253, 1958.
8. DREIZEN, S., SNODGRASSE, R. M., DREIZEN, J. G. and SPIES, T. D.: Seasonal distribution of initial appearance of postnatal ossification centers in hand and wrist of undernourished children. J. Pediat. 55:738, 1959.
9. SPIES, T. D., DREIZEN, S., SNODGRASSE, R. M., PARKER, G. S. and CURRIE, C.: Skeletal maturational progress of children with chronic nutritive failure. A.M.A. J. Dis. Child. 85:1, 1953.
10. SPIES, T. D., DREIZEN, S., SNODGRASSE, R. M., ARNETT, C. M. and WEBB-PEPLOE, H.: Effect of dietary supplement of nonfat milk on human growth failure. A.M.A. J. Dis. Child. 98:157, 1959.
11. PARKER, G. S., DREIZEN, S. and SPIES, T. D.: A cephalometric study of children presenting clinical signs of malnutrition. Angle Orthodontist 22:125, 1952.

CLINICAL STUDY

1-Phenethylbiguanide—an Orally Administered Hypoglycemic Agent

STANLEY S. BERGEN, JR. AND WILLIAM S. NORTON, II*

St. Luke's Hospital, New York

1-Phenethylbiguanide (DBI, phenformin) is an orally administered hypoglycemic agent which is not related to the sulfonylurea drugs.

DBI has been effective in treating diabetic subjects who require small amounts of insulin and as an adjunct to insulin therapy in the labile diabetic patient; however, the high incidence of gastrointestinal side effects it produces limits its use.

No systemic toxicity following administration of DBI has been noted in man.

The authors present their experience with DBI in treating 49 patients, and describe current theories concerning its mechanism of action.

In 1957, Ungar, Freedman and Shapiro[1] described the hypoglycemic action of an orally administered nonsulfonylurea preparation, N[1]-β-phenethylformamidinyliminourea (DBI or phenformin), in alloxan-diabetic animals. At the same time, Pomeranze, Fujiy and Mouratoff[2] published results of studies of the use of DBI in diabetic patients. This paper summarizes our experience with this agent in the Diabetes Clinic of St. Luke's Hospital, New York.

Material and Methods

Fifty-four diabetic patients were given DBI as part of their treatment regimen. Forty-nine diabetic patients, given DBI as part of their treatment, were observed for at least three months or until side effects of the drug prevented further evaluation. Initially, all patients were hospitalized for regulation of their diabetes, but, as it became evident that DBI caused relatively no toxicity, treatment with this preparation was extended to the Diabetes Clinic. All subjects were studied for evidence of renal, hepatic and hematopoietic abnormality before, during and after DBI therapy. Patients on insulin were maintained on a constant regimen. Blood sugar levels were measured by the Somogyi-Nelson method,[3] and the patients tested their own urine for reducing substance from one to four times a day with Benedict's solution.

Phenformin was administered as 25 mg. and 50 mg. tablets three times a day with meals as an insulin supplement; it was given

*Department of Medicine, St. Luke's Hospital, New York, New York.

STANLEY S. BERGEN, JR.

WILLIAM S. NORTON, II

four times a day with meals and at bedtime when used as the only form of antidiabetic therapy. Side effects were minimized when the tablet was ingested during the course of a meal. When gastrointestinal complaints or anorexia occurred, they often abated on omission of one or two doses of the medication.

The ages of the patients in this series ranged from 16 to 85 years (average of 49.9 years). Fourteen patients had labile-type diabetes. Duration of diabetes was estimated as being from a few weeks to 22 years. Thirty of the 54 patients had required insulin in amounts of 10 to 85 units per day. The remaining 24 either had tried dietary control of glycosuria or were in the group in whom initial diabetic control was attempted with diet and DBI. The criteria by which response to DBI was graded were as follows:

1. Good: Fasting blood sugar 60 to 150 mg. per cent; glycosuria 2 plus or less.
2. Fair: Fasting blood sugar less than 200 mg. per cent; no glycosuria over 3 plus.
3. Poor: Fasting blood sugar over 200 mg. per cent; frequent glycosuria.

Results

Gastrointestinal complaints developed in four patients before the effectiveness of DBI could be ascertained. In three patients, hyperglycemia proved to be too mild to warrant further treatment with biguanide.

In 23 patients hyperglycemia was controlled by DBI alone; in 15 the insulin requirement was lowered, and in many instances the course of the diabetic condition was stabilized by addition of DBI to the therapeutic regimen. Of the 23 patients receiving DBI alone, 15 displayed good control and eight had fair or poor control, as outlined in table 1. Metahexamide (100 to 250 mg.) or tolbutamide (500 to 1000 mg.) was added to the regimen of these eight patients; control of hyperglycemia improved in five and there was no change in three. Twelve of the patients receiving DBI and insulin together attained good control of hyperglycemia, while three achieved fair control.

Eleven patients failed to show a significant response to biguanide therapy. One patient had a total pancreatectomy and was unable to tolerate a sufficient dosage of DBI to control the hyperglycemia. Nausea or vomiting or both developed in 10 patients before an appreciable change in blood sugar was noted, despite relatively high dosages of biguanide.

Side effects included nausea and anorexia in 12 patients, vomiting in seven, diarrhea in two, metallic taste in one, and dizziness in one. These symptoms were observed in 18 of the 54 patients (33 per cent of cases), and occurred up to three months after the medication was begun. In 12 subjects, the symptoms of gastrointestinal distress were so severe that they could not be overcome, and hyperglycemia could not be controlled by varying the dosage schedule or using antinauseants. Slight reduction of the dosage of DBI circumvented side effects in six patients without compromising diabetic control. Two patients on DBI alone were observed to have occasional acetonuria without glycosuria while in caloric balance. Symptoms suggestive of hypoglycemia were noted in two patients on DBI and insulin. Both were seen by a local physician and improved when given orange juice. No chemical confirmation of hypoglycemia was obtained in either patient.

Of the 29 patients who are still receiving DBI after from 6 to 24 months of therapy, 16 are using the biguanide as the sole therapy in addition to diet, and 13 are taking it to supplement insulin treatment or in conjunction with a sulfonylurea preparation. Using the criteria noted previously, good control has been maintained in 23 of this group and fair control in six during this period. Those pa-

TABLE 1

USE OF DBI IN TREATING 49 PATIENTS WITH DIABETES MELLITUS

THERAPY AND RESULTS	PATIENTS (NUMBER)
DBI plus diet	23
Control	
Good	15
Fair	4*
Poor	4*
DBI and insulin plus diet	15
Control	
Good	12
Fair	3
Failures	11
Side effects without therapeutic response	10
Total pancreatectomy	1
Side effects (including failures)	26†
Side effects overcome by reducing dosage	8
Gastrointestinal symptoms	6
Acetonuria	2

*Addition of sulfonylurea to the regimen improved the control in five patients; control remained unchanged in three.

†DBI was discontinued in 18 of these patients.

tients on DBI alone require a daily dosage of 50 to 200 mg. per day, the average being 100 mg.; those who are also taking insulin or a sulfonylurea are receiving 25 to 100 mg. per day, the average being 60 mg.

Discussion

The patients in this study were selected because (1) they presented difficult problems in management, (2) their diabetes showed a labile course, (3) they required small amounts of insulin, or (4) they were poorly controlled by diet alone. When all failures in treatment, including those due to side effects, were considered, DBI aided in controlling hyperglycemia in 63 per cent of the series. Unfortunately, the occurrence of side effects usually made it impossible to increase the total daily dosage of DBI above 250 mg.; thus, it could not be determined whether in some instances hyperglycemia would have been overcome with larger dosages of the biguanide.

The most satisfactory responses to DBI have been obtained in subjects requiring small amounts of insulin for regulation of diabetes[4-7] or when this agent has been used as an adjunct to insulin therapy in labile diabetes.[8-12] DBI has been reported effective and able completely to replace insulin in certain juvenile diabetic patients.[7-10] Five patients in the present series were in this category. One was controlled by DBI alone; two were stabilized by DBI, and two were unable to tolerate the biguanide in doses sufficient to control hyperglycemia. Skillman, Kruger and Hamwi,[12] using DBI alone, were unable to control hyperglycemia in a patient who had had pancreatectomy, and our depancreatized patient was unable to tolerate sufficient medication to determine whether the diabetic state could be controlled by DBI alone.

Because its duration of action seems to be about five hours, DBI must be taken in divided doses. There seems to be a cumulative dosage level of 150 to 200 mg. per day, above which side effects occur with great frequency. These side effects have an over-all incidence of from 35 to 60 per cent.[6-9] Full cooperation of the patient, close follow-up by the physician, administration of the medication with meals, and a slow stepwise increase of the dosage by no more than 25 mg. every two to three days may help reduce the incidence of side effects. No systemic toxicity other than that associated with gastrointestinal upset has been reported in man to date.[6-10]

In accordance with the suggestion of Beaser,[13] sulfonylurea therapy was combined with DBI in eight patients who achieved less than satisfactory control on the biguanide alone. Since two orally administered hypoglycemic drugs have different modes of action, it was hoped that their cumulative effect might be sufficient to control hyperglycemia which was not adequately controlled by DBI alone. Five of the eight patients showed improved control while on combined orally administered medications. Further study of this combined therapy with DBI and the sulfonylureas is needed before the efficacy of such an approach can be evaluated.

Mechanism of Action

N^1-β-phenethylformamidinyliminourea is a water-soluble biguanide with a maximal hy-

poglycemic action in man at five hours. It is effective in man[3-12] and in most animals, including the eviscerated guinea pig, the alloxan-diabetic rat, rabbit and monkey.[1] Death in animals following administration of DBI has resulted from hypoglycemia[1] and cardiac arrhythmias.[14]

Wick and Stewart,[15] using the rabbit, recovered 90 per cent of the administered dose of C^{14}-labeled DBI in the urine in 24 hours, with tissue concentration localized in the liver and gastrointestinal tract prior to its excretion. DBI has a structural similarity to other biguanides such as PALUDRINE® hydrochloride (N_1-parachlorophenyl-N_5-isopropylbiguanide), which has not been reported to have a hypoglycemic action.[16] It is chemically related to the hypoglycemic agent SYNTHALIN® A, a guanidine,[17,18] which was given clinical trials as an orally administered hypoglycemic agent 30 years ago but found to be hepatotoxic. Although no systemic toxicity has been noted in man following administration of DBI, Creutzfeldt and Moench,[19] using greater than therapeutic doses in guinea pigs, demonstrated mild degranulation and vacuolation of pancreatic alpha cells and minimal degenerative changes in the liver and kidney.

Hollunger[20] believes the guanidines act by blocking the oxygen uptake of the mitochondria through inhibition of phosphorylation. This action promotes an anaerobic state in the peripheral tissues. Randle and Smith[21] noted that under such anaerobic conditions glucose rapidly enters the cells in the absence of insulin.

Fajans and associates,[22] who carried out detailed studies in patients receiving DBI, found no significant alteration in their glucose tolerance, insulin sensitivity or hyperglycemic response to glucagon. Bergen, Hilton and Norton[23] and Fajans and associates[22] noted no effect of DBI on adrenal function. Lambert[10] described slight depression of the radioiodine uptake in patients on DBI therapy, but these changes reverted to normal after longer periods of treatment.

The apparent lack of an endocrine effect has led most investigators to consider anaerobic glycolysis as a possible mechanism of action of DBI.[5,24-27] Craig, Miller and Woodward[25] demonstrated that fasting blood lactate levels and excretion of urinary lactate increased after DBI was given to diabetic patients. These subjects also showed a higher and more prolonged blood lactate response to infusion of sodium lactate than did diabetic patients receiving insulin. Fajans and associates[22] observed a delay in the disappearance of pyruvate and lactate from the blood in diabetic patients receiving DBI who were studied by means of glucose tolerance and pyruvate tolerance tests.

This apparent increase in traffic over the pathway from pyruvate to lactate may result from the DBI-induced inhibition of tricarboxylic acid cycle oxidation, with an associated increase in anaerobic regeneration of diphosphopyridine nucleotide (DPN) from dihydrocoenzyme I (DPN. 2H). Steiner and Williams[26] believe that they have demonstrated such a block at the cytochrome oxidase level, while Wick, Larson and Serif[27] place the major site of interference in the succinic oxidase system. Both groups of investigators have noted inhibition at various enzyme levels in the tricarboxylic acid cycle, depending on biguanide concentration, and this variable may well account for the conflicting evidence concerning the drug's site of action. Ungar, Psychoyos and Hall[28] have recently shown that DBI affects oxidation phosphorylation by mitochondria by acting directly on DPN-dependent steps in a competitive manner to block enzyme activity. Since the concentration of DBI used in many of these studies was greater than the concentration obtained with therapeutic dosages, it may well be that enzyme inhibition has very little to do with DBI's mode of action.

Butterfield, Fry and Holling,[29] measuring peripheral arteriovenous glucose differences in man, showed that there is increased peripheral utilization of glucose after administration of DBI. Tranquada, Kleeman and Brown[30] studied diabetic patients by catheterization of the right hepatic vein and the femoral artery for four hours following oral administration of DBI. They were unable to demonstrate any change in hepatic glucose or urea output or

oxygen consumption by the liver, but they did note increased peripheral utilization, as indicated by a fall in arterial glucose levels.

Animal studies also have disclosed accumulation of lactic acid in the blood, decreased muscle glycogen, and decreased muscle oxygen consumption after administration of DBI.[31] Glucose uptake by rat diaphragm increases following addition of DBI to the medium,[32] while animals fed alanine and DBI have diminished liver glycogen and urinary nitrogen, compared with controls, suggesting a decrease in gluconeogenesis.[31]

REFERENCES

1. Ungar, G., Freedman, L. and Shapiro, S. L.: Pharmacological studies of a new oral hypoglycemic drug. Proc. Soc. Exper. Biol. & Med. 95:190, 1957.
2. Pomeranze, J., Fujiy, H. and Mouratoff, G. T.: Clinical report of a new hypoglycemic agent. *Ibid.*,[1] p. 193.
3. Nelson, N.: A photometric adaptation of the Somogyi method for determination of glucose. J. Biol. Chem. 153:375, 1944.
4. Williams, R. H., Tanner, D. C. and Odell, W. D.: Hypoglycemic actions of phenethyl-, amyl- and isoamylbiguanide. Diabetes 7:87, 1958.
5. Nielsen, R. L., Swanson, H. E., Tanner, D. C. and Williams, R. H.: Effects on blood sugar of a new potent hypoglycemic compound. A.M.A. Arch. Int. Med. 101:211, 1958.
6. Hall, G. H., Crowley, M. F. and Bloom, A.: Oral treatment of diabetes. Brit. M. J. 2:71, 1958.
7. Odell, W. D., Tanner, D. C., Steiner, D. F. and Williams, R. H.: Phenethyl-, amyl- and isoamylbiguanide in the treatment of diabetes mellitus. A.M.A. Arch. Int. Med. 102:520, 1958.
8. Krall, L. P., White, P. and Bradley, R. F.: Clinical use of the biguanides and their role in stabilizing juvenile-type diabetes. Diabetes 7:468, 1958.
9. Krall, L. P. and Bradley, R. F.: Clinical evaluation of formamidinyliminourea, a new biguanide oral blood sugar-lowering compound: Comparison with other hypoglycemic agents. Ann. Int. Med. 50:586, 1959.
10. Lambert, T. H.: Clinical observations with a new oral hypoglycemic agent (DBI). Clin. Res. 6:92, 1958.
11. Lundbaek, K., Nielsen, K. and Rafaelsen, O. J.: The mode of action of oral antidiabetic compounds. Lancet 1:1036, 1958.
12. Skillman, T. G., Kruger, F. A. and Hamwi, G. J.: Metabolic and endocrine studies with phenethyldiguanide. Diabetes 8:274, 1959.
13. Beaser, S.: Therapy of diabetes mellitus with combinations of drugs given orally. New England J. Med. 259:1207, 1958.
14. Wick, A. N. and Larson, E. R.: Studies with phenethyldiguanide, a hypoglycemic agent. Clin. Res. 6:91, 1958.
15. Wick, A. N. and Stewart, C. J.: Tissue distribution of administered DBI and its relationship to DBI action. Clin. Res. 7:111, 1959.
16. Schmidt, L. H., Hughes, H. B. and Smith, C. C.: On the pharmacology of N_1-para-chlorophenyl-N_5-isopropylbiguanide (Paludrine). J. Pharmacol. & Exper. Therap. 90:233, 1947.
17. Bodo, R. and Marks, H. P.: Relation of Synthalin to carbohydrate metabolism. J. Physiol. 65:83, 1928.
18. Staub, H. and Küng, O.: Zum Synthalinmechanismus. Klin. Wchnschr. 7:1365, 1928.
19. Creutzfeldt, W. and Moench, A.: Vergleichende Untersuchungen mit den blutzuckersenkenden Guanidinderivaten Synthalin B und Phenyläthyldiguanid (DBI). (Ein Beitrag zur Frage der sog. A-Zellgifte.) Endokrinologie 36:167, 1958.
20. Hollunger, G.: Guanidines and oxidative phosphorylation. Acta pharmacol. et toxicol., supp. 1, 11:7, 1955.
21. Randle, P. J. and Smith, G. H.: Regulation of glucose uptake by muscle. I. The effects of insulin, anaerobiosis, and cell poisons on the uptake of glucose and release of potassium by isolated rat diaphragm. Biochem. J. 70:490, 1958.
22. Fajans, S. S., Moorhouse, J. A., Doorenbos, H., Louis, L. H. and Conn, J. W.: Metabolic effects of phenethylformamidinyliminourea (DBI) in normal subjects and in diabetic patients. Clin. Res. 6:252, 1958.
23. Bergen, S. S., Hilton, J. G. and Norton, W. S.: Effects of phenethylbiguanide on adrenal function and responsiveness as measured by ACTH test. Proc. Soc. Exper. Biol. & Med. 98:625, 1958.
24. Tyberghein, J. M. and Williams, R. H.: Metabolic effects of phenethyldiguanide: A new hypoglycemic compound. Proc. Soc. Exper. Biol. & Med. 96:29, 1957.
25. Craig, J. W., Miller, M. and Woodward, H., Jr.: The influence of DBI on the metabolism of lactic acid in diabetic patients. American Diabetes Association, San Francisco, 1958.
26. Steiner, D. F. and Williams, R. H.: Respiratory inhibition and hypoglycemia by biguanides and decamethylenediguanidine. Biochim. et biophys. acta 30:329, 1958.
27. Wick, A. N., Larson, E. R. and Serif, G. S.: A site of action of phenethylbiguanide—a hypoglycemic compound. J. Biol. Chem. 233:296, 1958.
28. Ungar, G., Psychoyos, S. and Hall, H. A.: Action of phenethylbiguanide, a hypoglycemic agent, on tricarboxylic acid cycle. Metabolism 9:36, 1960.
29. Butterfield, J., Fry, I. K. and Holling, E.: Effects of insulin, tolbutamide and phenethylbiguanide on peripheral glucose uptake in man. Diabetes 7: 449, 1958.
30. Tranquada, R., Kleeman, C. and Brown, J.: The acute effects of DBI on human hepatic intermediary metabolism. Clin. Res. 7:110, 1959.
31. Williams, R. H., Tyberghein, J. M., Hyde, P. M. and Nielsen, R. L.: Studies related to the hypoglycemic action of phenethyldiguanide. Metabolism 6:311, 1957.
32. Bolinger, R. E., McKee, W. P. and Davis, J. W.: Comparative effects of DBI and insulin on glucose uptake of rat diaphragm. Metabolism 9:30, 1960.

SCIENTIFIC EXHIBIT

Emergency Care of the Eye

LEO L. MAYER

Chief Ophthalmologist, Veterans Administration Center, Jackson, Mississippi

THE philosophy of medicine demands that the physician treat the patient to the best of his ability. Sight is frequently maintained at normal values when emergency care is of the best; and the older the patient, the more care that is necessary.

Most emergency conditions of the eye are first seen by the general practitioner, and the practitioner who is well prepared to care for these emergencies inspires the confidence of his patient. There are many procedures that will enable the physician to save sight, relieve pain, and recognize cases that should be referred to an ophthalmologist. The ophthalmologist appreciates the worth of his colleagues who he knows are well prepared to render adequate emergency care.

William Fox, Chief Photographer, Veterans Administration Center, Jackson, Mississippi, assisted the author with the illustrations.

General Principles of Management

The necessary means for adequate care of an emergency condition of the eye are simple and inexpensive. The three most important requirements are:

Comfort for the Patient

Patient should lie relaxed on a comfortable examining table or a bed. An injection of ½ gr. codeine sulfate will relieve ocular pain and general discomfort. Only contraindication is in cases of known or suspected head or brain injury, as the drug may confuse the complete physical examination.

If anesthesia is necessary for treatment, a 0.5 per cent PONTOCAINE® hydrochloride solution may be dropped on the conjunctiva of the lower lid. To get the drops into the eye when the patient is squeezing, pour at inner canthus, then pull down lower lid. A 2 per cent Pontocaine Eye Ointment may be spread on the lash margins of the lids with a cotton applicator. Cocaine is no longer used, because it softens the cornea and deteriorates in solution.

Use of dropper bottle for applying Pontocaine solution.

Pontocaine applied with cotton applicator.

Illumination

An ordinary gooseneck lamp with 150 W bulb and a bull's-eye condenser, which fits on lamp-stand, gives the best illumination.

Magnification

A loupe that magnifies two to three times and may be worn like eyeglasses or over regular glasses allows examiner free use of his hands. The lighted magnifiers are impractical.

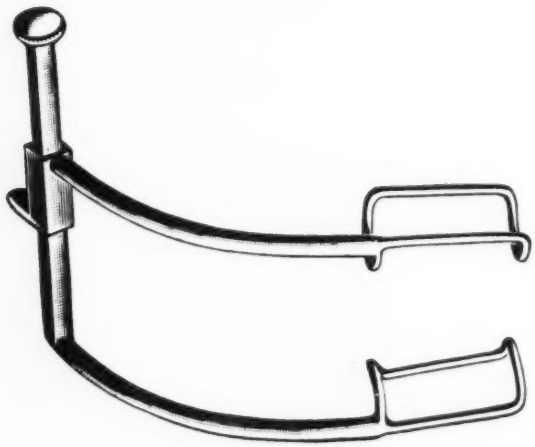
Other Equipment for Management

Ophthalmoscope

Practice leads to perfection in the use of this important instrument. The anterior segment of the eye is best seen with a plus 12 convex lens, which magnifies the pupillary reaction to light.

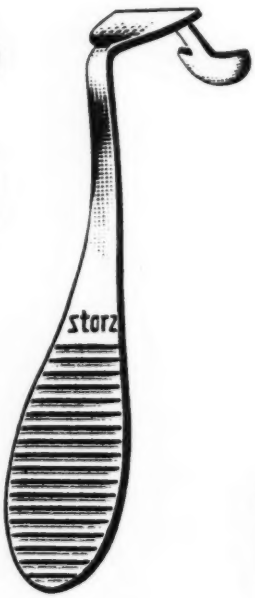
As the amount of plus lens is decreased, first the iris, then the vitreous humor, and finally the retina, choroid, optic nerve, and blood vessels are seen magnified about 15 times. If the pupil is small, no harm is done by dilating it.

Speculum



The Murdock speculum, a springless type that opens the eyelids without tension, is best.

Lid Evertor



A lid evertor of metal or plastic is useful in examining the upper cul-de-sac.

Lid Clamp

A lid clamp with a complete back prevents the needle from perforating the globe. The front of the clamp is open.

Equipment *(continued)*

Small Kelly clamp

Small forceps

Bard-Parker blade with sharp point

Sharply beveled hypodermic needle on 2 cc. Luer syringe

Curved cutting needle

4-0 chromicized catgut

4-0 silk suture

Small cotton applicators

Medication

Topical anesthetic: 0.5 per cent Pontocaine hydrochloride (tetracaine hydrochloride).

Anesthetic for injection: 2 per cent XYLOCAINE® hydrochloride (lidocaine hydrochloride).

Anesthetic for eyelids: 5 per cent Xylocaine Ointment, 2 per cent Pontocaine Eye Ointment, or 2 per cent BUTYN® sulfate.

To dilate pupil: 4 per cent homatropine in 1 per cent PAREDRINE® hydrobromide, 2 per cent homatropine hydrobromide, 2 per cent EUPHTHALMINE®, 2 per cent CYCLOGYL® hydrochloride, or 1 per cent MYDRIACYL® (new and best).

To reduce tension of globe in suspected glaucoma: 2 per cent pilocarpine hydrochloride.

To stain cornea: 2 per cent fluorescein sodium in 2 per cent soda bicarbonate or in strips.

To treat infection of anterior segment: 30 per cent sodium sulfacetamide, or 10 per cent sodium SULAMYD® Ointment, or both.

Steroids: Topical use is in the experimental stage. When used for lesions of the conjunctiva and cornea, especially in dendritic ulcer and epithelial erosion of the cornea, the lesions heal more slowly.

Intramuscular and intravenous injections have given amazing results in herpes zoster, anterior and posterior uveitis, and in some cases of retrobulbar neuritis, especially when the etiology is unknown.

General Principles of Treatment

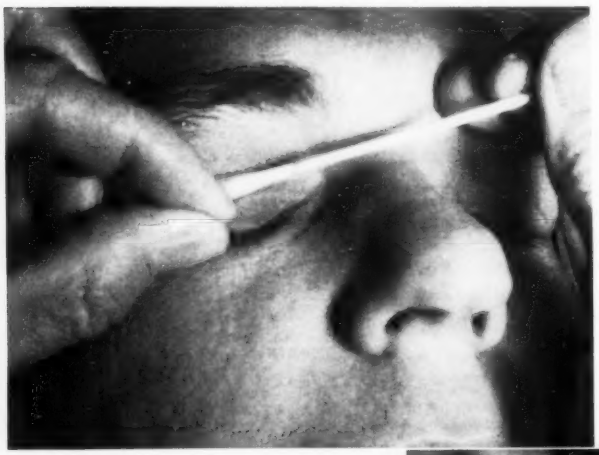
Vision of *both* eyes should be estimated. If Snellen or Jaeger charts are not available, ordinary book print read at the usual reading distance will suffice.

In all injuries, the size and clearness of *both* pupils should be thoroughly investigated.

In contusions or concussions, look for blood in lower portion of anterior chamber and, if possible, use ophthalmoscope to see if a red reflex may be obtained; if it is black, this probably indicates a hemorrhage into the entire globe.

No local anesthetic, in either solution or ointment form, should be prescribed for the patient to use.

Following any abrasion, removal of foreign body, burn, and even injury to the eye, sodium sulfacetamide in a 30 per cent solution or 10 per cent ophthalmic ointment should be prescribed to prevent secondary infection.



Method of turning upper lid, first phase.

Method of turning upper lid, second phase.

Use of lid evertor in turning upper lid, first phase.

Use of lid evertor in turning upper lid, second phase.

Use of thumb in exposing lower cul-de-sac.

Specific Treatment

Incisional wound

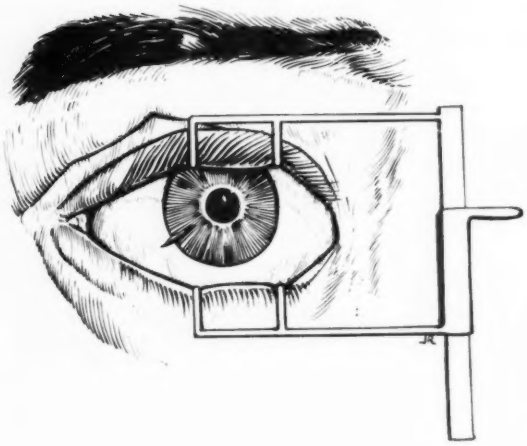
In incisional wounds of the lid, immediate repair without debridement is best. Repair should be done layer by layer, from inside out: conjunctiva, tarsus, orbicularis muscle, then skin of lid.

Inject damaged lid with 2 per cent Xylocaine. Use curved cutting needle threaded with 4-0 chromicized catgut for all layers except skin, which is closed with interrupted suture, using 4-0 silk. An ordinary small Kelly clamp is used as a needle holder. A lid clamp, when closed on damaged lid, will prevent bleeding and will present and firm up tissues that are being treated.

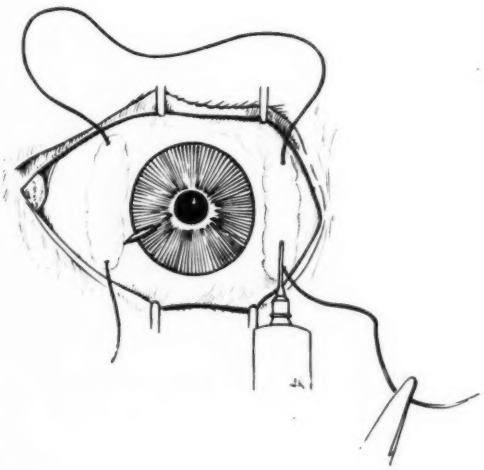
Undermining edges of skin to a distance of 1 to 2 mm. aids in inserting needle and tying knot just outside incision. A continuous mattress suture with 4-0 silk tied on the skin side is quickly inserted, effects proper return of function of orbicularis muscle and lid, and is easily removed.

Specific Treatment

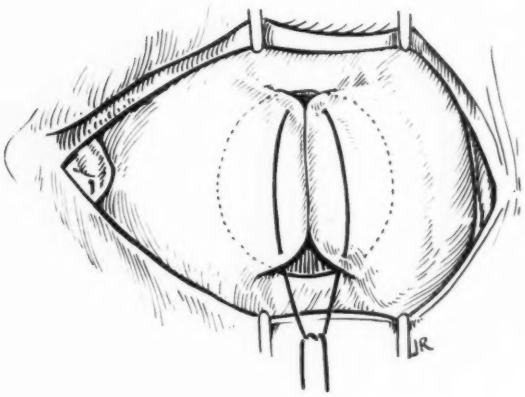
Incisional wounds of the sclera and cornea should be seen by the ophthalmologist as soon as possible. Meanwhile, instead of bringing a conjunctival flap over the wound, the following procedure prevents exposure of the globe to infection. When suture is released, the epithelium of the conjunctiva prevents adhesion.



Anesthetize topically with Pontocaine, 3 drops at two minute intervals, until conjunctiva is insensitive to needle prick.



Undermine and balloon up the conjunctiva on either side of the cornea, using a 2 cc. syringe filled with 2 per cent Xylocaine.



Close over wound area with a purse-string suture, using 4-0 black silk.

Foreign body

When foreign body is in conjunctival sac, administer topical anesthetic; then expose upper cul-de-sac, using lid evertor. Stain cornea with fluorescein, applied with cotton (never gauze) applicator, to determine whether or not epithelium has been denuded. If it has, apply 10 per cent sodium Sulamyd Ointment and cover with an eye patch for 24 hours.

If pupil of injured eye is smaller than that of uninjured eye, which sometimes occurs due to secondary iritis, a drop of 2 per cent homatropine hydrobromide is indicated.

When foreign body is embedded in cornea, administer topical anesthetic; then expose area, using speculum. Test degree of anesthesia by touching lightly the conjunctiva outside the corneal area. If needle is felt, add another drop of Pontocaine; wait one minute and test again.

With good illumination and a loupe, the depth of the embedded matter is easily estimated, and the foreign body may be removed with a sharply beveled hypodermic needle on the end of a 2 cc. Luer syringe. Puncture of the globe has never been reported in the literature by this procedure, so be determined.

Removal of embedded foreign body in cornea.

If all the rust does not come out in the first attempt, apply 2 per cent homatropine and 10 per cent sodium Sulamyd Ointment, cover with a patch, and wait 24 hours. Any discomfort may be relieved with aspirin, a barbiturate or a sedative. See patient again in 24 hours, reanesthetize, stain globe with fluorescein, and remove softened rust.

Concretions or calcium deposits sometimes push through the conjunctiva, especially in elderly persons, and feel like a foreign body in the eye. These are easily removed with a sharp-pointed Bard-Parker blade. No further care is necessary.

An eyelash lodged in the lower punctum may turn in toward the cornea and conjunctiva, causing a constant irritation. It is easily and quickly removed without anesthesia, using a small forceps.

Specific Treatment

Burns

Flash burns are very painful, because the epithelium of the cornea is completely denuded and the nerve endings are exposed. The entire cornea stains with fluorescein. Topical administration of 0.5 per cent Pontocaine at one minute intervals and application of ice-cold packs to the lids give relief in 5 to 10 minutes. Healing occurs in three to six hours without any special medication. Steroid drops applied locally are contraindicated.

Hot oil or grease splashed into the eye often denudes the epithelium of the cornea or conjunctiva or both. The injured area should be treated with a topical anesthetic and 2 per cent homatropine to prevent secondary iritis, then covered with an eye pad.

The best way to remove chemicals, such as acids and alkalies, from the eye is to put the patient's head under the tap and flush the eye vigorously with water.

Secretion in eyes of newborn

This condition may be due to failure of nasal end of nasolacrimal duct to open. Instill 30 per cent solution of sodium sulfacetamide (never boric acid), and then press on lacrimal sac just below the lacrimal duct near the nose. If condition does not clear in a week's time, refer patient to ophthalmologist.

Thick pus in the eyes of a newborn is most often due to gonorrhea. Patient should be hospitalized and an ophthalmologist consulted.

Diseases of the eye

DIFFERENTIAL DIAGNOSIS OF IRITIS, GLAUCOMA AND CONJUNCTIVITIS

	IRITIS	GLAUCOMA	CONJUNCTIVITIS
Pain	Severe	Severe	Slight, if any
Pupil	Small	Dilated	Normal
Cornea	Clear	Steamy	Normal
Redness	Circumcorneal	Variable	Marked
Iris	Muggy	Muggy	Normal
Aqueous humor	Cloudy	Cloudy	Normal
Eyeball	Soft	Hard	Normal
Nausea	Infrequent	Not unusual	Never
Headache	Frequent	Frequent	Never
Vision	Some loss	Marked loss	Normal

Treatment

IRITIS: ½ gr. codeine sulfate, by injection; 2 per cent homatropine. Never use atropine.

GLAUCOMA: ½ gr. codeine sulfate, by injection; 2 per cent pilocarpine hydrochloride; 250 mg. DIAMOX®, by mouth.

CONJUNCTIVITIS: 30 per cent sodium sulfacetamide, drops during day and ointment at bedtime.

CLINICOPATHOLOGIC CONFERENCE

Report From Veterans Administration Hospital, Hines, Illinois

Edited by William J. Donnelly, M.D., Chief, Section of Hematology

Case Report

A 71 YEAR old Negro man, a retired railroad attendant, was admitted to Hines Veterans Administration Hospital on December 23, 1959, because of acute urinary retention of 24 hours' duration, with only occasional dribbling. The patient stated that he constantly felt like voiding and had continual pain low in the abdomen. He had first noted slowing of the urinary stream two or three years earlier, and he had had nocturia three to four times per night for several months before admission. He had no history of hematuria, burning on urination, chills, or fever, and he denied ever having had gonorrhea or syphilis.

The patient stated that his general health had been good otherwise, except for partial hemiplegia of the left side, which had developed gradually six months before his admission to Hines. He had no other neurologic complaints. His weight had remained at a constant 200 lb. He denied the use of both alcohol and cigarettes, but he smoked three or four cigars daily. His medical history included a herniorrhaphy in 1914.

Physical examination conducted on admission showed that the patient's blood pressure was 130/80, pulse 100, temperature 99.2° F., and respirations 24. He appeared obese and was alert and cooperative. The lungs were clear to auscultation and percussion. The heart rate was 100, with regular rhythm and no murmurs. Abdominal examination was difficult because of the patient's obesity; no masses were palpated. Rectal examination disclosed that the prostate was enlarged and firm, and it was thought that benign hypertrophy was present. Neurologic examination revealed weakness of the left side of the face and of the left leg.

Laboratory data—Hematologic studies showed that the hemoglobin was 14.2 gm.; the hematocrit was 45 per cent, and the white blood cell count was 6000. Urinalysis revealed a specific gravity of 1.010, 4 plus albumin, and no sugar; microscopic examination showed numerous red blood cells. Nonprotein nitrogen on December 24 was 40.5 mg.; on December 30, it was 38 mg. Glucose was 88 mg.; alkaline phosphatase was 2.4 and acid phosphatase was 0.5 Bodansky units. Serologic studies gave negative results. An electrocardiogram on December 24 and a chest x-ray five days later showed no abnormalities.

An intravenous pyelogram on December 29 revealed bilateral excretion of the dye; the right kidney was displaced superiorly and laterally. In addition, the right ureter was displaced medially, suggesting a large mass, perhaps extrarenal. A radiolucency in the pelvis of the right kidney was thought to represent a filling defect within the pelvis or a duplication of the collecting systems, with some superimposition simulating a filling defect. The distal right ureter was redundant and flexed on itself. The visualized portion of the bladder was displaced superiorly. The

left kidney appeared small, and the left ureter also was somewhat redundant. Retrograde pyelography was recommended.

Hospital course—Shortly after admission, the patient was catheterized, and 985 cc. of urine was obtained. A urethral catheter was inserted, and the bladder was irrigated, with closed drainage. Gross blood was returned on irrigation. On December 31, cystoscopy was performed, and a moderately heavy amount of hemorrhage was noted coming from the mucosa of the prostatic urethra. Severe prostatic hypertrophy was present. Because of the moderately heavy bleeding, the examination was terminated and the bladder was irrigated extensively. The patient appeared to tolerate the procedure well.

On January 6, the patient suddenly had a severe seizure which involved his entire body and lasted about three to four minutes. He did not lose consciousness, and it was thought at that time that he had had a grand mal seizure. He was given 1 gr. phenobarbital immediately, and 0.5 gr. phenobarbital four times daily was prescribed. On the following day, the patient again had a seizure, with pronounced jerking of the left arm and leg. He was given 8 cc. paraldehyde intramuscularly.

The patient's temperature remained essentially normal, and on January 9 and for a part of the following day he was asymptomatic. On January 10, he suddenly drew his head back and had jerking movements of his entire body. His eyes were rigidly staring, and his respirations became labored. Cyanosis, pulse irregularity and severe weakness rapidly followed. The patient died within 10 minutes.

Discussion

DR. RICHARD O. BURNS (senior resident, surgical service): Initially, this patient appeared to have a urologic condition. His history was compatible with benign prostatic hypertrophy. The only other complaint was that of progressive hemiplegia of the left side. This was described as a partial hemiplegia of the left side. What is meant by partial hemiplegia? The patient probably had slowly progressive hemiparesis of the left side.

In addition, examination revealed a weakness of the left side of the face. Was this a central or a peripheral type of facial weakness? In the peripheral type, due to a lesion involving the nucleus of the seventh nerve or the facial nerve itself, all the facial muscles are affected, including the orbicularis oculi and the frontalis. In the central type, due to a lesion in the cortical motor strip, the eyes and forehead are spared. The usual explanation is that the upper facial musculature has a bilateral cortical representation. I assume that this patient had a central type of facial weakness, in which the eyes and forehead were not affected. In addition, he had weakness of the left leg, and the left arm also was probably weak, although this was not mentioned.

The general physical examination did not reveal any remarkable findings. The only abnormality seen on neurologic examination was the weakness of the left side of the face and of the left leg. It would have been most helpful if the specific negative observations had been described. Was the weakness spastic or nonspastic? Were the deep tendon reflexes normal? The visual fields, results of the funduscopic examination, and the quality of the carotid pulses were not described. These factors are important in ruling out a vascular lesion. A massive vascular lesion ordinarily produces not only hemiparesis of the left side, but it also often causes a hemianesthesia on that side. The patient did not have a lumbar puncture, and neither x-rays of the skull to determine pineal shift nor an electroencephalogram was made. He was considered to have an acute, emergent urologic condition with acute urinary retention.

After cystoscopy and drainage by catheter, the patient did well until January 6, when he had what was described as a grand mal seizure involving the entire body. No one saw the beginning of that first seizure, but it could have begun in the left arm and leg as a jacksonian type of seizure. The seizure on the following day was accompanied by a severe jerking of the left arm and leg, and this was almost certainly a jacksonian seizure. The fact that the patient did not lose consciousness during the first two seizures also indicates that they were of this type.

The results of most of the laboratory tests were either normal or negative. The intravenous pyelogram, however, showed displacement of the kidney upward and laterally, as well as radiolucency in the right renal pelvis. Thus, this patient had roentgenographic evidence suggestive of a retroperitoneal mass, a sudden onset of acute urinary retention, and hemiparesis and jacksonian seizures of the left side.

Now, we should consider the differential diagnosis of seizures. The most common is the idiopathic type of seizure, but this is usually the grand mal type. This patient had jacksonian seizures. Were they uremic, hypoglycemic or toxic seizures? He did not have uremia; his blood glucose was normal, and he was not toxic. Local irritation of the cerebral cortex is the most likely cause of jacksonian seizures. This patient had no specific symptoms or signs suggestive of an expanding intracranial lesion. He had no headaches, nausea or vomiting; he did not complain of visual disturbances, and he was not ataxic. However, he may have had a small, localized lesion which had not yet caused a generalized increase in intracranial pressure. The differential diagnosis of a space-occupying lesion is a lengthy one, and I would like to discuss the most likely causes of such a lesion.

Let us first consider the vascular lesion. Did an earlier stroke cause the hemiparesis in this patient? I think not. This was a progressive hemiparesis of the left side. Strokes do not ordinarily produce a slow, steady progression of neurologic deficit. Could this man have had a slow narrowing of the lumen of one of the carotid arteries? This conceivably could cause a slowly progressive neurologic deficit, but not one involving only the motor strip. The carotid artery supplies the entire anterior part of the brain from the parietal region forward. One branch helps to supply the visual area. If this man had an occlusion of the carotid artery, he should have had a sensory deficit as well as a motor deficit and possibly a visual field defect. Another vascular lesion to consider is the subdural hematoma. It is not unusual to see this lesion without history of trauma; however, a subdural hematoma with a six month history of slowly progressive hemiparesis of the left side, without mental clouding or other changes, is not likely. Could this man have had a venous thrombosis of either the surface cortical veins or the superior sagittal sinus? I consider this a remote possibility. He may have had a chronic cystitis, with septic embolization through a patent foramen ovale to the brain, but this occurs rarely. A septicemia, with thrombosis of the cortical veins and a brain abscess involving only the motor cortex, is possible but not likely. The patient remained afebrile during his hospital course. Could he have had an arteriovenous malformation or a hemangioma? Unfortunately, no one listened to his head for a cephalic bruit. An arteriovenous malformation or a hemangioma could explain the slowly progressive symptoms, the jacksonian seizures, and the patient's sudden death. These lesions are uncommon and usually cause trouble much earlier in life.

It is entirely possible that this man had a primary brain tumor. However, we must not forget the roentgenographic evidence of a retroperitoneal mass. If he did have a primary brain tumor, what type would he have had, with a history of slow progression, of seizures, and of no increased intracranial pressure? A meningioma is the most probable; an oligodendroglioma and a number of others are lesser possibilities.

Metastatic tumors of the cortex of the brain notoriously cause jacksonian seizures. They may do this long before there is any evidence of increased intracranial pressure. If this patient had a metastatic brain tumor, where was the primary lesion? Of all tumors which metastasize to the brain, bronchogenic carcinoma leads the list. In one large series, bronchogenic carcinoma accounted for 54 per cent of all metastatic brain tumors. Hypernephroma accounts for up to 20 per cent of all metastatic brain tumors. In this case, we must think of a retroperitoneal tumor which metastasized to the brain. The lymphoma group of tumors is the next best possibility. Less likely are adrenal tumors or a rhabdomyosarcoma of the psoas muscle.

This patient had a retroperitoneal mass,

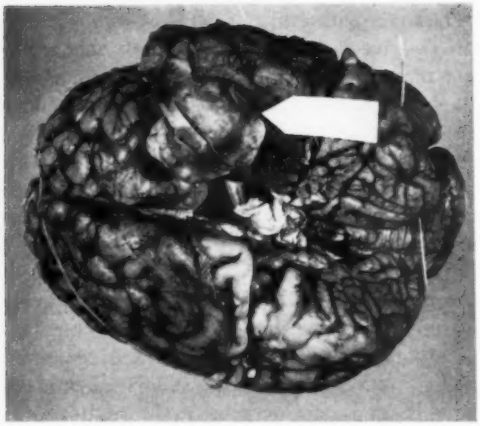


FIGURE 1. Photograph of brain, showing meningioma (arrow) adjacent to right frontoparietal cortex.

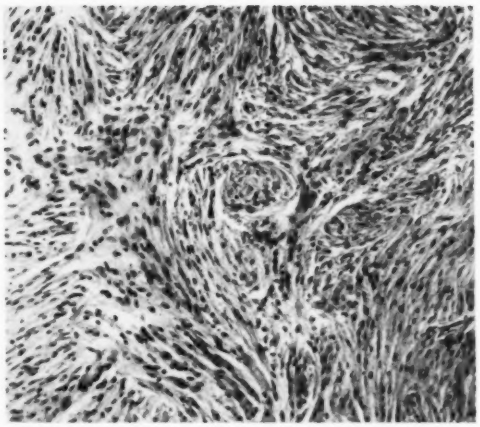


FIGURE 2. Photomicrograph of meningioma, showing the meningotheliomatous appearance characterized by islands of uniform cells with surrounding dense, collagenic fibers.

pushing the kidney superiorly and laterally. I think it arose in the kidney. There also was a radiolucency in the pelvis of the kidney, compatible with growth of a tumor in this region. I think that he had a hypernephroma which had metastasized to the brain. The terminal episode might have been caused by a hemorrhage into the tumor, with herniation of the brain stem.

DR. MYRON E. RUBNITZ (chief, laboratory service): Dr. Burns, have you ever seen a patient with a metastatic brain tumor, developing over this period, who had a normal hemoglobin and no sign of debilitation?

DR. BURNS: Yes, I have seen several patients with metastatic brain tumors who did not show general debilitation. I saw one recently who had had a bronchogenic carcinoma removed two years previously and who came in with posterior cranial fossae symptoms of pronounced ataxia. He had a metastatic tumor the size of a large lemon in the cerebellum; however, he had had no weight loss. We removed the tumor, and he is doing quite well.

DR. RUBNITZ: Since you have mentioned the possibility of bronchogenic carcinoma, we should see the x-rays.

DR. MIRIAM LIBERSON (physician-in-charge, diagnostic radiology service): The chest film showed no abnormalities except for a tortuous aorta and degenerative changes in the dorsal spine. Intravenous pyelography showed no definite evidence of a retroperitoneal mass; there was only a suggestion of a mass. Retrograde pyelography was recommended for better visualization of the pelvicalyceal structures of the right kidney. In my opinion, the only positive finding was the elevation of the bladder, which would suggest a large prostate.

DR. LIONEL BERNSTEIN (assistant director, professional services for research): I would like to ask Dr. Burns a question regarding sensory disturbances with classic hemiplegia or hemiparesis. Usually, only the radiation from the motor cortex is involved, but if the lesion is extensive the radiation from the sensory cortex is similarly affected. Usually, patients are at first in coma. They cannot be tested, and so we are unaware of how often they have sensory defects. As they recover, the motor deficit remains, whereas the sensory capacity usually returns. Would you comment on the value of the presence or absence of a sensory deficit in differentiating a vascular lesion from a space-occupying lesion?

DR. BURNS: As I recall, I was talking about occlusive disease in a large artery, not in the lateral striate artery supplying the internal capsule. Progressive occlusion of the carotid artery or the middle cerebral artery could explain a progressive neurologic deficit. How-

ever, if there is an occlusive disease of the carotid artery or of one of the larger vessels, more than just the motor strip should be affected. The middle cerebral artery or its branches, the anterior choroid or lateral striate arteries, supply the entire internal capsule (along with some overlap from the posterior cerebral artery), a good part of the basal ganglions, the optic tracts in some cases, and the entire sensorimotor cortex. A tumor, however, may more readily produce very circumscribed signs at first, and only later cause a greater neurologic deficit. After a stroke, sensation may return after a period, although motor function remains impaired. I might add that seizures are not common late in vascular disease. Perhaps Dr. Tigay would tell us how often he sees seizures associated with a thrombosis involving the internal capsule.

DR. ELI L. TIGAY (chief, neurologic service): Seizures may occur at the onset of a cerebrovascular lesion. They occur most frequently in the onset of a cerebral or subarachnoid hemorrhage, less frequently in a cerebral embolism, and least frequently in a cerebral thrombosis. I believe that the incidence of seizures in cerebral hemorrhage may be as high as 15 per cent.

DR. RUBNITZ: At autopsy, the major finding was a globular mass measuring 5 cm. in diameter, lying over and compressing the right frontoparietal cortex, and apparently arising from the covering leptomeninges. The gross appearance of the mass was characteristic of meningioma (figure 1). There was little evidence of brain damage and minimal herniation in the area of the brain stem. This encapsuled mass was easily separated from the cortex.

Microsection of the tumor revealed it to be the common meningotheliomatous type of meningioma, characterized by islands or sheets of cells, some showing a palisading arrangement. The surrounding stroma was composed of thick, collagenous fibers, often in a fascicular arrangement (figure 2). All the cells had a uniform appearance, with no apparent mitotic activity.

The kidneys were normal. The prostate was enlarged, weighing over 200 gm. Microsections showed marked benign hypertrophy and hyperplasia.

Bailey and Bucy[1] recognized nine types of meningiomas, based on the predominating arrangement and type of cells. These types are mesenchymal, angioblastic, meningotheliomatous, psammomatous, osteoblastic, fibroblastic, melanoblastic, sarcomatous and lipomatous. Other classifications of meningiomas have been devised, one of which correlates the anatomic site with the symptoms and neurologic findings.

Although an overwhelming majority of these tumors are intracranial, a few cases of meningioma located within the nasal cavity have been reported. Some believe that this rare occurrence is a result of a developmental abnormality in which misplaced arachnoid elements act as the anlage of the meningiomas in this area. However, others believe that meningiomas within the nasal cavity are extensions from parent tumors arising within the skull. Within the past few months here at Hines, we have diagnosed a nasal tumor as meningioma. At that time there was no indication of any intracranial lesion. The patient was being treated by the psychiatrists. We felt that this was truly a primary nasal meningioma. However, only a few weeks ago, the neurosurgeons made another angiogram and found more elevation of the anterior cerebral artery than was seen in the angiogram made three months earlier. A frontal flap was turned, and an intracranial meningioma was found lying along the cribriform plate on both sides of the falx and extending into the right nasal cavity.

DR. BURNS: In neurosurgery, all you can do is to diagnose the presence of a space-occupying intracranial lesion. You have to turn a flap to find out what it is. However, meningiomas frequently can be strongly suspected, since there is sometimes calcification on the meninges next to the calvaria. Plain x-rays of the skull would perhaps have been very valuable in this case.

REFERENCE

1. BAILEY, P. and BUCY, P. C.: The origin and nature of meningeal tumors. Am. J. Cancer 15:15-54, 1931.

The Physician in the Caricature

HELMUTH NATHAN,* JOSEPH HIRSH† AND NESRIN BINGOL

Albert Einstein College of Medicine, New York

THROUGHOUT history the human being has been the subject of enduring interest to the artist. The single corporate facet of the human being which we might call his emotional posture has been of particular interest. Man's moods and feelings, his needs, loves and angers, his strengths and weaknesses, his piety and arrogance, his agony and inspiration, and his hope and despair are reflected most often in his face and, with subtler nuance, in what Plato has called "the mirror of his soul"—his eyes. Face and eyes tell us a great deal more about man than do his physical habitus, manner and walk. From the most primitive time onward, the artist has recognized this fact and has transmitted these insights to the viewer wherever and whatever his disciplines may be. This he has done in two ways: by reproducing the normal form into a portrait and by abstracting the essentials, eliminating the unimportant components, and intensifying basic characteristics in what is called a caricature.

A caricature is something more than purely amusing, though it may indeed be that, too. It is often linear or graphic satire, invective, castigation, or derogatory statement of emphasis. The caricature was known among the ancient Egyptian, Indian, Grecian and Roman artists. Leonardo da Vinci in the caricature of the caricature (opposite page) was probably the first to give an intellectual analysis of this art form. The artists who followed him gave added emphasis, meaning and insights into the psychology and philosophy of this field of art. Psychologists such as Freud, Kris and Gompertz, to be sure, added further insights, but the basic contributions to the psychology of caricature were made by two Frenchmen, Baudelaire and Bergson.

To understand the nature of caricature, one must understand the nature of the comic and laughter. One is a necessary ingredient of the other. It may be involuntary or intentional. The key to its form is its prime characteristic of contradiction. In the caricature, the comic element often results from a strange collision of feelings and surprise, and the undermining of superiority, prideful delusions, and unassailable intelligence.

*Clinical Professor of Surgery; †Associate Professor of Preventive and Environmental Medicine, Albert Einstein College of Medicine, New York, New York.

Leonardo da Vinci: Caricature. Windsor Castle, Royal Library.

Baudelaire and Bergson have described different types of the comic. The simple type leads to simple caricature, which is generally grotesque but harmless. Intentional caricature is often aggressive, hostile, caustic and full of violence. Whether simple or intentional, in one way or another, the caricature is an instrument of judgment and evaluation. In the political, social and professional arenas, it is often used as an instrument of attack or defense. By ridiculing a person or an idea, prestige may be undermined, status jeopardized, and position altered. Contrariwise, prestige, status and position may be enhanced and improved by caricature. The caricature, therefore, becomes something more than an instrument in the hands of the interpretive artist. The artist himself becomes and often is a person whose skills can shape or destroy an idea, a person or a profession.

The presentation of the natural in an exaggerated or unnatural way may become in its untruthfulness more characteristic than a true portrait. To be truly effective, the caricature must be translucent, yet shades of meaning and nuance have their place in this medium. Thus, the caricature does not appeal to us solely on an intellectual basis, but on an emotional one as well. Its impact goes beyond and deeper than our consciousness. Innately, we may rebel against the abhorrent or the grotesque; we may reject the pain which it so graphically portrays, yet we will smile and laugh at the caricature.

The physician and the medical profession have come in for their share of caricaturing throughout history. The positive role which the physician plays in the lives of his patients, in health and sickness, in sadness and despair, and in birth and death is portrayed in various art forms. In the caricature, however, the physician's humanness and vulnerability, his ineptness and fallacies, and his apparent preoccupation with financial gain are most forcefully and revealingly expressed. In various other art forms—plays, novels, essays—Molière, Voltaire, Busch, Shaw and others have taken the physician to task. But it has remained for the caricaturist and for many who are not pre-eminently caricaturists but artists, such as Leonardo, Michelangelo, Jan Steen, Brouwer, Brueghel and others, to highlight the physician and the medical profession in all their defect—real and imagined. Interestingly enough, the caricature also very often reveals specific characteristics of temperament, as well as the artist's national origins. These are particularly prominent in the examples which follow.

William Hogarth, 1697-1764. Called the "writer with the brush and pencil," Hogarth was to graphic art what Jonathan Swift was to literature. His pictures, expressing his critical and polemic thinking, were sharp, aggressive attacks on a weak, dispirited and hostile society. He painted well and produced an enormous number of portraits, still lifes, and studies of people in their daily work and personal relationships. He portrayed the poor and the rich and the high and the low of society; he amused himself and others with the *parvenues* and prostitutes, the beautiful and the grotesque.

Physicians came in for their share of ridicule. "The Anatomical Theatre," shown here, is an aggressive work. Its composition, architecture and grouping are beautiful; its draftsmanship is remarkable, but its basic idea is destructive and undermining to the prestige of physicians. The dog getting the extras seems to be the only happy creature.

Thomas Rowlandson, 1756-1827. A representative of the new romantic movement of the eighteenth century, Rowlandson employed masterful technic and precision in his art form to criticize society. Using the etching needle with water color, he produced aquatinted plates of translucence and beauty. Although trained and educated in England, he showed the effects of French influence in that he had a real *joie de vivre*, a love of excitement and money-spending. He was basically unacademic, strong in his judgments, sympathies and antipathies, and extremely critical of the ethical conduct of others.

His caricatures of doctors are particularly caustic. He portrayed the physician primarily as a money-maker. That is the theme of the plate depicted here, which shows the physician emptying the trouser pockets of his dying patient. This caricature is aptly entitled "Simple Methods."

Honoré Daumier, 1808-1879. A prodigious craftsman, Daumier's works number in the thousands. His lithographies were unrestrictedly beautiful. In a sense, Daumier was a pioneer in political lampoonery. He was aggressive and amusing in his attacks and was personally fearless. The threat of imprisonment and starvation did not stay his pen. He lived for the ideal of freedom in political and private life. Looking for the all too human element, he found in the human face a range of character, expression and emotion that few artists have matched. Sympathy for the poor and simple and the devoted and humble is apparent in many of his caricatures, and reflects the influence of Balzac and Goya. Caricaturist par excellence, he posed a strange paradox in warning artists to abstain from this form of art, citing it for all of its ugliness.

In this caricature, the physician represents the registrar itemizing the cost of each disease so that he may add to his already overflowing coffer.

Collection, Museum of Modern Art, New York.

George Grosz, 1893-1959. Grosz is considered one of the greatest artists of our time. A strange combination of antagonistic forces formed his character. Although he was a typical, well-educated Prussian, with good manners, respect for others, and a willingness to help, he rebelled against German self-pride and aggression.

His greatest period, that of World War I and the postwar years, is seen in the series entitled "The Face of the Ruling Class, Capitalism and Prostitution." In the plate illustrated, the army physician is one of the class of mentally imprisoned men who will do anything to maintain their status and prestige in a circle to which they want to belong. The highest circle of German *bourgeoisie* and aristocracy was the officers corps. In this caricature, the physician is willing to declare a skeleton fit to fight in the front line. The self-admiring officers, the orderly and military policeman, and the compliant and obedient subaltern are all stereotypes.

Despite a pen dipped in acid, Grosz numbered many physicians among his close personal friends. He was, in fact, an enthusiast of the Albert Einstein Art in Medicine Program. (Pages 422 to 426 in the October 1960 issue of POSTGRADUATE MEDICINE.)

Marcel Vertes, 1895- . Among the best known of contemporary caricaturists is the American-Hungarian artist, Vertes, who consistently ridicules that much-maligned group of physicians, the psychoanalysts. He is the master of factual, impressive drawings. Many persons know him from the tablecloth drawings in the famous Toulouse Lautrec film, "Moulin Rouge."

Typical of his caricatures is the one shown here in which an analyst looking in the mirror asks himself how he feels today, a stereotype repeated with many variations.

"Now tell me all about myself."

Reproduced from: Vertes, M.: It's All Mental. New York, Tudor Publishing Co., 1959.

Self-help Devices:

Selection of Wheel Chairs

Consideration of Specific Disabilities

EDWARD W. LOWMAN AND HOWARD A. RUSK

Institute of Physical Medicine and Rehabilitation
and the Arthritis Self-help Device Office*

New York University Medical Center, New York

The Amputee

THE selection of one type of wheel chair for the amputee in preference to another of the three models available† depends on whether the patient is to be fitted with a prosthesis or prostheses. Some persons recommend the Traveller chair (figure 1) for the patients with bilateral above-the-knee amputations who do not plan to use prostheses. The contention is that the large wheels in front counterbalance the loss of body weight from the hips down. However, we have found that since the patient must shift forward to propel the wheels he is safer in an amputee chair in which the axles are set back about 2½ in. (inset) and the large wheels are in back (figure 2).

Some authorities believe that a chair with detachable arms is contraindicated, because the impaired trunk balance increases the danger of falling during transfer. They contend that when the arms of the chair are used for support the detachable armrests are less stable than fixed arms, and that there is the danger of the patient's forgetting to lock the armrests securely.

We feel that detachable rather than fixed arms are best, because they are automatically offset and therefore provide an extra 1½ in. seat width to accommodate the prostheses, and they permit the patient to transfer both sideways and forward. The emphasis should be on having well-functioning armrest locks

*Supported at the Institute by the Arthritis and Rheumatism Foundation.

†Illustrated in the August 1960 issue, pages 198 and 199.

and on making the patient aware of the importance of checking these locks before moving off or onto the chair.

The Arthritic

The average arthritic will fare well in a wheel chair with a standard back, large wheels in the rear, hand brakes, removable footrests, and detachable arms. Severe physical disability and deformity often make it necessary to consider the prescription more individually.

The patient with rheumatoid spondylitis, e.g., ankylosis of the spine and hips, may require a chair with a reclining back and an additional headrest extension (figure 3). The patient in figure 4 is ankylosed in his entire spine, hips, knees and ankles. As a result of his flexion deformities, he is unable to reach the standard low footrests and he has no range of motion for maneuverability once he is lodged in the sitting position. With the footrests specially raised to a level above the front caster wheels, his feet are stabilized in a firm position. The addition of a 4 in. seat cushion and a 2 in. back cushion provides sufficient spring to give him some maneuverability in the sitting position.

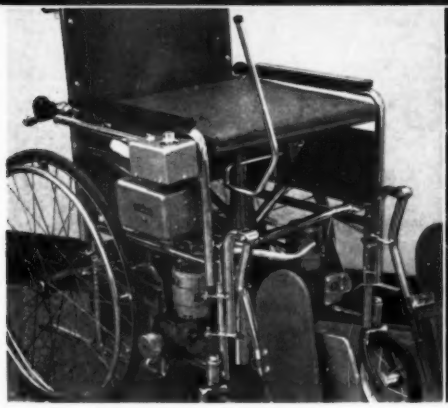
Patients with arthritis are prone to limited mobility at the hip and knee joints, and often find it difficult to sit down to and arise from the seats of standard wheel chairs, which are about 20 in. from the floor. If only minimal increase in seat height is needed, the seat can be raised with cushioning. If this is insufficient, a hydraulic elevating seat (figure 5), which provides a range of from 20 to 29 in. from the floor, may be necessary. This often makes the difference between the patient's being completely wheel chair-bound and being capable of getting in and out of the chair for minimal walking. Severe flexion contractures in the upper extremities may make it impossible for the patient to reach the wheels for self-propulsion, and a motorized chair may then be the only alternative (figure 6).

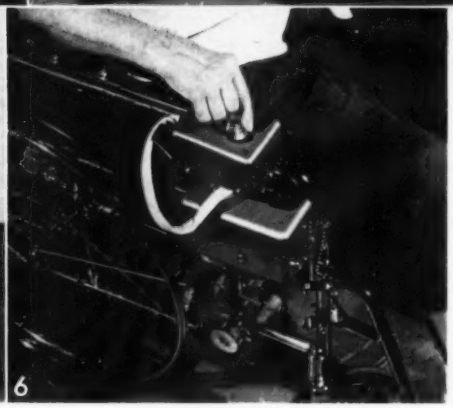
The Arthrogrypotic

Persons who have congenital multiple deformities must be fitted with a wheel chair that compensates for loss in joint range of motion and unequal extremity lengths. The patient in figure 7 manages best in a motorized chair because he has considerable difficulty in reaching the wheels for self-propulsion.

2

3




6

The Hemiplegic

This patient usually does well in a standard wheel chair, which is successfully propelled with the "good" hand and foot (figure 8). In order to pedal, the foot must reach the floor squarely; thus the height of the chair seat is important. Hemiplegics who are short in stature often do well in the 16 in. junior-sized chair.

A one arm-driven chair (figure 9) enables the individual with one disabled

arm or hand to guide and propel the chair with the "good" arm or hand. Two hand rims, one smaller than the other, are located on one side of the chair. The inner or larger rim is connected to the opposite wheel by a folding axle. When both hand rims are grasped together, the chair may be propelled forward or backward in a straight line. When either hand rim is moved independently, the chair will turn left or right in response to the hand rim used. In our experience, however, we have found that propulsion of this chair is mechanically more difficult than is that of other chairs, especially when there is residual mental confusion from the cerebral injury.

The Paraplegic and Quadriplegic

The paraplegic usually does well with a standard wheel chair with detachable arms and swinging, detachable footrests.

The quadriplegic often needs a chair with a full-reclining back; detachable, upholstered armrests; padded, elevating legrests, and antitipping levers. The latter are essential to prevent the chair from tipping when the patient is in the full-reclining position. The full-reclining back permits the patient to be completely supine for rest periods without having to be removed from the chair. With the chair maximally inclined (180 degrees), some quadriplegics can transfer to the bed with limited or no help by using the "body roll." In such cases, the big wheels should not protrude above the chair seat. The lowered wheels, however, may be out of the patient's reach, making it impossible for him to propel himself. One must decide then whether it is more important for the patient to propel himself or to transfer to the bed with a minimum of help.

If there is some residual shoulder muscle power but weakness of the hands, the patient may successfully propel the wheel chair if vertical projection knobs (figure 10) are added to the outer rim. Again, when there is no alternative, a motorized chair with a single button control may be the only means of the patient's getting about unassisted.

This is the last of a series of six articles on wheel chair prescriptions, prepared to assist the physician in the selection of the chair, accessories and modifications that will most usefully serve his patient. For a more detailed discussion of the relationship of the wheel chair to activities of daily living, we recommend "Physical Rehabilitation for Daily Living," written by E. Buchwald, in collaboration with Drs. H. A. Rusk, G. G. Deaver and D. A. Covalt, and published by the Blakiston Division, McGraw-Hill Book Company, Inc., New York, Toronto and London.

Combined reprints of this series are available on request to Dr. Edward W. Lowman, Institute of Physical Medicine and Rehabilitation, 400 East 34th Street, New York 16.

Editorials

Postgraduate Medicine

Editor-in-Chief:
CHARLES W. MAYO, M.D.

Contributing Editor:
MORRIS FISHBEIN, M.D.

Executive Editor:
SYLVIA COVET

PALLIATIVE OR NONPALLIATIVE: A SURGICAL PROBLEM

At the conclusion of every single or multiple stage operative procedure, the surgeon—whatever his field or specialty—should write a description of the purpose of the operation, the steps in the technic used, and the positive or negative findings noted during the course of the procedure. Only by such a standard method is it possible for the surgeon to judge his own work or for others to evaluate his way of accomplishing its purpose.

What a surgeon strives for, once a patient comes under his care, is definitive cure, correction or positive palliation of the condition involved. For the surgeon who deals with a malignant condition, concern with palliation begins with the question of whether or not he considers the condition cured. At this point a "gray zone" may well confront the surgeon, for the end point is not always black or white. Here, too, there may be some confusion regarding spoken and published reports of statistical findings and classifications and interpretations of them. No one likes this state of affairs: it can lead to error; it can lead to adoption of a technically poor or even a bad operation; it can lead to errors in teaching, and it can be the basis of ill-designed research.

Is it possible to decide correctly whether or not an operation in the gray area is palliative, and so avoid the pitfalls mentioned, or must we live with these uncertainties and use them as excuses for agreeing or disagreeing with our colleagues' reports as given at medical meetings or published in medical journals?

Even considering the chance of error in this gray area, I think there is amazing agreement between the conscientious surgeon's estimate of cure and the five year survival rates. Opinion must be based on a multitude of factors, not just on intuition. For example, manual exploration through an incision in the left lower quadrant will not establish whether one or more lumps in the liver are malignant; proof is possible only when a specimen is obtained with an accurately placed Silverman needle and biopsy is performed.

To the surgeon who deals with malignancy, nothing is more pleasing than, at the conclusion of an operation, to be able to tell a patient's family and friends that, in his opinion, the operation has been successful and a cure may be expected. The patient, his family, his friends, and the surgeon all descend into

the depths when an operation has been totally unsuccessful or but palliatively successful.

Just as we have various grades of malignancy, based on differentiation of cells, and classifications of extent of spread, based on degree of confinement or spread of malignant tissue, so too we might define prognoses more precisely than as either cure or palliation.

Cure expresses confidence that the particular condition for which the patient underwent operation has been eradicated. Palliation implies hopelessness, with only a guess as to the time of certain demise from the disease. What I am looking for is a word which will leave not only the patient, family and friends, but also the surgeon, with the hope of cure and without the inference signified by palliation. No one cherishes uncertainty, but the word I seek should describe the gray area.

Perhaps the law of chance now operates in such manner that the majority of reliable surgeons who have accepted cure and palliation as the only categories divide the gray area and place half of the uncertainties in each group. Maybe that is good enough!

If a word is important to express more exactly the situation of patients who, in the surgeon's opinion, fall into this zone of uncertain prognosis—where we are hopeful but "keep our fingers crossed"—that word might be *dubito*, which expresses the Latin phrase *quod dubites, aequum sit an iniquum* (about which you may be uncertain).

CHARLES W. MAYO

THE PERIL OF DELAY IN PUBLISHING

ACCORDING to the *Archives of Ophthalmology* for November 1960, Dr. Ben Jenkins, a small-town American practitioner, began using α-chymotrypsin for releasing tissues in cataracts in 1955. He attempted to clear vitreous opacities in a congenitally blind man with this enzyme but was unsuccessful. The enzyme did, however, cause the lens to dislocate. Thereafter, Dr. Jenkins began using α-chymotrypsin routinely for cataract extractions, but failed to report it in a medical publication. Two years later, Dr. Joaquin Barraquer made a similar observation and reported it in 1958.

This incident is reminiscent of the first use of ether by Crawford Long, of Georgia (which is, incidentally, the state of residence of Dr. Jenkins). Long lost much of the credit to William Thomas Green Morton, Boston, who published his results.

MORRIS FISHBEIN

WITNESSES IN FORENSIC MEDICINE

IN 1952 the life of Sir Bernard Spilsbury was published under the title "The Scalpel of Scotland Yard."[1] It recounted Spilsbury's early medical education and his services as what was characterized as "the incomparable witness." This provides an excellent description of British medical jurisprudence and the part played in it by Sir Bernard, who was a great British pathologist with records of some 25,000 postmortem examinations.

More recently published and released last fall in the United States is the autobiography of Sir Sydney Smith,[2] entitled "Mostly Murder." Sir Sydney is characterized on the jacket of the book as the greatest living authority on forensic medicine in Great Britain. Following his early days in New Zealand and his student days at Edinburgh, he went to Egypt during the first World War, where he became principal medical expert to the Ministry of Justice. In 1928 Sir Sydney returned to Edinburgh as professor of forensic medicine. His career included many important medicolegal cases, in which he frequently was an opponent to Sir Bernard Spilsbury.

In Sir Bernard's biography there is but one reference to Sir Sydney, in connection with a case of murder involving strangulation. Apparently Sir Bernard saw the body while it was still fresh. Sir Sydney studied the specimens later, and he tried to convince the jury that Sir Bernard did not know the difference between postmortem discoloration and a bruise. Sir Sydney claimed that the findings described by Sir Bernard were not visible when he saw the specimens. However, in his autobiography, Sir Sydney reveals an intense dislike for Sir Bernard, making quite uncomplimentary re-

marks about him. For instance, he says, "Spilsbury seemed lacking in all the warmer human attributes with which Willcox [another expert] was so well endowed." In discussing another case in which he opposed Sir Bernard, he says, "A clash of experts always makes the jury skeptical about the whole scientific evidence." In the case in which manual strangulation was alleged to be the cause of death, the evidence conflicted with Sir Sydney's belief that strangulation should be accompanied by a fracture of the hyoid bone; in this case the hyoid bone had not been fractured during strangulation but was fractured by Sir Bernard while he was removing it. Sir Sydney says, "In the course of the years I had learned a number of lessons in giving evidence in court. One was to confine one's answer to the question asked; another was not to try to score off counsel. I had also found that it pays to be reticent, and to keep back a few odds and ends to release under cross-examination; this makes the opposing advocate more careful in his approach."

A great responsibility of a medical witness is emphasized in these sentences: "Perhaps Spilsbury did not fully realize that fame brings responsibility as well as honor. I do not think the jury would have returned the verdict they did if his evidence had been given by anyone else but Spilsbury." Perhaps the following remarks by Sir Sydney are a little too venomous for an unprejudiced colleague. "Spilsbury is dead now, and his death was tragic. At the inquest on his last case of suicide—and there was no room for doubt this time—he was the deceased. I mourned him sincerely, for we had lost a man of outstanding brilliance and complete integrity. He was so often right that he could almost be forgiven for being so stubborn when he was wrong. One might almost hope that there will never be another Bernard Spilsbury."

Of these two books I find the autobiography of Sir Sydney Smith much more fascinating than the biography of Sir Bernard Spilsbury; it brings out the drama of the expert witness much better. The foreword by Erle Stanley Gardner, our most prolific writer of detective stories, is in itself a brilliant essay on the performance of expert witnesses. Perhaps one of Mr. Gardner's concluding paragraphs deserves a wide circulation. He says, "If the public could only realize the importance of having well-trained experts in the field of legal medicine, of having medical examiners who are absolutely impartial, thoroughly competent, and well paid not only in terms of financial returns but in the compensation of human dignity and appreciation, we should have fewer unsolved murders and fewer innocent men wrongfully convicted."

MORRIS FISHBEIN

REFERENCES

1. Browne, D. G. and Tullett, E. V.: The Scalpel of Scotland Yard. New York, E. P. Dutton & Co., Inc., 1952.
2. Smith, S.: Mostly Murder. New York, David McKay Co., Inc., 1959.

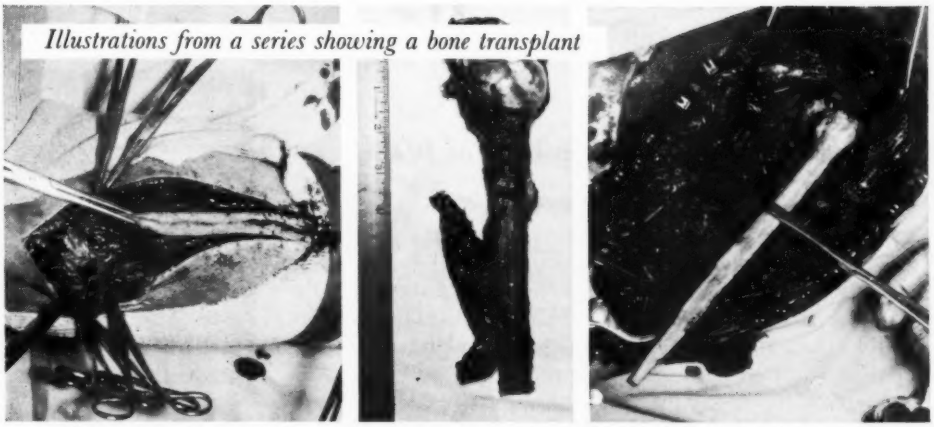
STRANGE WORDS

The editors of the supplementary volume of the "Oxford English Dictionary," in preparing a new edition, are endeavoring to find the time when certain words which have application directly to medicine were first used in scientific or other writings. The words with the approximate dates when they were first introduced are listed below. Many of the dates assigned seem to be much too late, at least to my own memory. In any event, if anyone wants to be helpful to the editors of the supplementary volume of the "Oxford English Dictionary," he may submit his evidence on these words to them at 40 Walton Crescent, Oxford, England: marijuana, marihuana (1894); microcurie (1931); microradiography (1913); Mongol—person afflicted with mongolism (1926); mother-figure (1953); mother-fixated (1958); mother-fixation (1934); neurosurgeon (1929); neurosurgery (1904); neurosurgical (1934); nucleoprotein (1907); nutritionist (1934); occupational therapy (1922); oestrin-biochemistry (1928); oestrogen (1939); oestrogenic (1936); oestrone (1938), and oestrous cycle (1920).

MORRIS FISHBEIN

Pictures that tell the story sharply:

Illustrations from a series showing a bone transplant



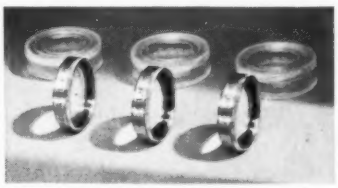
Elliptical incision excising old biopsy wound.

Excised segment of the humerus with attached biopsy wound.

Graft held in place against the wound of the left arm.

. . . because the Kodak Retina Reflex S Camera has through-the-lens viewing and ground-glass focusing

You see the subject natural size and get exactly what you see on the full-area ground glass. Critical sharpness is assured by either ground-glass or rangefinder focusing with five interchangeable lenses—28mm to 135mm. Correct exposure every time . . . the automatic exposure-control links the extra-sensitive photoelectric meter with the diaphragm of every lens. Automatic depth-of-field indicator. Many other precision features assure extra-fine-quality work with greater handling ease. Specialized photo aids greatly extend the camera's scope to such fields as ultra close-ups (see above) and photomicrography. Price, Kodak Retina Reflex S Camera, *f*/2.8, $199.50.



Kodak Retina Close-Up Lens Set, Type R, for pictures from 11 to 6 inches film-to-subject distance.

Price is list and subject to change without notice.

For full information about this expert camera, see your Kodak photographic dealer or write:

Kodak
TRADE MARK

EASTMAN KODAK COMPANY, *Medical Division*, Rochester 4, N. Y.

Serving medical progress through Photography and Radiography

News of Interstate

Priestley Named President-Elect of IPMA

JAMES T. PRIESTLEY

DR. James T. Priestley, Mayo Clinic, Rochester, Minnesota, was named president-elect of the Interstate Postgraduate Medical Association at the 1960 Assembly in Pittsburgh. Dr. Priestley is professor of surgery at the University of Minnesota Graduate School of Medicine, Rochester-Minneapolis. He was graduated from the University of Pennsylvania School of Medicine, Philadelphia, in 1924 and began his fellowship in surgery at the Mayo Foundation, Rochester, in 1928.

Vice-Presidents and Board Member Elected

SHEPARD KRECH, JR.

CLAYTON T. NOONAN

ROGER A. PEATEE

Vice-presidents for the ensuing year are Dr. Shepard Krech, Jr., Easton, Maryland; Dr. Clayton T. Noonan, Seattle, and Dr. Roger A. Peatee, Bowling Green, Ohio.

Dr. Nels A. Hill, Madison, was named to the Board of Trustees. He will succeed Dr. Raymond G. Arveson, Frederic, Wisconsin, who died on June 5, 1960.

1961 Program to Feature Color Television

Plans are under way for the 1961 Assembly in Cleveland, November 13 to 16. Color television programs, which will be featured in the teaching sessions, will be prepared by staff members of the Cleveland Clinic.

Dr. William D. Holden, professor and head of the department of surgery at Western Reserve University School of Medicine, Cleveland, will serve as president of the 1961 Assembly.

Research Awards Presented

Special cash awards for meritorious research were presented to Drs. Sil H. Lee and Maxwell P. Westerman, members of the faculty of the University of Pittsburgh School of Medicine. Dr. Lee, of the department of surgery, was recognized for his research on "The physiologic and pathologic effects of porta-caval shunt." Dr. Westerman, instructor in medicine, was selected for his research on "Lipid alterations in the aging red cell."

Attendance Awards

At the Pittsburgh meeting, 21 physicians received attendance awards. These special certificates are presented to members who have attended 10 meetings of the Interstate Postgraduate Medical Association since 1940. Shown with some of the trustees and officers are:

Front row (*left to right*): Dr. C. A. Taylor, Batesville, Ark.; Dr. S. J. Smith, Bowling Green, Ohio; Dr. W. J. Copeland, Cary, Ill.; Dr. J. C. Schmidtke, Elgin, Ill.; Dr. C. H. Wolfe, Ambridge, Pa.; Dr. R. M. Arnold, Avon Lake, Ohio; Dr. Doris E. Dahlstrom, Kalamazoo; Dr. T. A. Spitler, Findlay, Ohio; Dr. M. R. Lorenzen, Toledo; Dr. R. A. Hill, Middletown, Ohio.

Back row (*left to right*): Dr. W. B. Hildebrand, Menasha, Wis. (trustee); Dr. Robert M. Zollinger, Columbus (president, 1950); Dr. William D. Holden, Cleveland (president, 1951); Dr. F. E. Williams, Jr., Tyler, Tex.; Dr. J. D. Merida, Cleveland; Dr. J. M. Siekierski, Griffith, Ind.; Dr. K. C. W. Dean, Caledonia, Ont.; Dr. T. H. Heenan, Detroit; Dr. V. W. Bair, Belle Vernon, Pa.; Dr. J. Mather Pfeiffenberger, Alton, Ill. (trustee); Dr. Donald C. Conzett, Dubuque, Iowa (trustee); Dr. Ben T. Whitaker, Boone, Iowa (trustee); Dr. Willis I. Lewis, Herrin, Ill. (trustee); Dr. Nels A. Hill, Madison (trustee); Dr. Robert N. Larimer, Sioux City, Iowa (trustee); Dr. Edwin S. Hamilton, Kankakee, Ill. (chairman, Board of Trustees).

Attendance award recipients not pictured: Dr. W. I. Easton, Selkirk, Man.; Dr. J. O. Milligan, Seattle; Dr. G. F. Peggs, Detroit; Dr. G. P. Riebel, Ashland, Ohio; Dr. K. S. Treiber, Erie, Pa.

Over 60 published papers since 1953...

COUMADIN®

the proven anticoagulant

FOR ORAL, INTRAVENOUS OR INTRAMUSCULAR USE

COUMADIN is the *original* and *only* warfari responsible for establishing this drug as closel approaching the ideal anticoagulant.[1,2]

stops tension

For neuralgias, dysmenorrhea, upper respiratory distress, and postsurgical conditions...new compound kills pain, stops tension, reduces fever—gives more complete relief than other analgesics.

Soma Compound is an entirely new, totally different analgesic combination that contains three drugs. First, Soma: a new type of analgesic that has proved to be highly effective in relieving both pain and tension.* Second, phenacetin: a "standard" analgesic and antipyretic. Third, caffeine: a safe, mild stimulant for elevation of mood. As a result, the patient gets more complete relief than he does with other analgesics. Soma Compound is nonnarcotic and nonaddicting. It reduces pain perception without impairing the natural defense reflexes.*

NEW NONNARCOTIC ANALGESIC

soma® Compound

Composition: Soma (carisoprodol), 200 mg.; phenacetin, 160 mg.; caffeine, 32 mg.
Dosage: 1 or 2 tablets q.i.d.
Supplied: Bottles of 50 apricot-colored, scored tablets.

NEW FOR MORE SEVERE PAIN

soma® Compound + codeine

BOOSTS THE EFFECTIVENESS OF CODEINE: Soma Compound boosts the effectiveness of codeine. Therefore, only ¼ grain of codeine phosphate is supplied to relieve the more severe pain that usually requires ½ grain. **Composition:** Same as Soma Compound plus ¼ grain codeine phosphate. **Dosage:** 1 or 2 tablets q.i.d. **Supplied:** Bottles of 50 white, lozenge-shaped tablets; subject to Federal Narcotics Regulations.

**References available on request.*

WALLACE LABORATORIES · Cranbury, N. J.

New *for your armamentarium*

Information published in this department is supplied by the manufacturers of the products described.

• ANESTHALUNG

DESCRIPTION: For use in surgery, this instrument aids in controlling the rate and volume of the patient's breathing. A pressure-sensitive volume control assures complete gas exchange in the lungs. While the system does not interfere with spontaneous breathing, it automatically delivers a preset volume of gas and controls the rate of respiration if the patient stops breathing or does not breathe deeply enough. The respiratory rate may be set for up to 60 times a minute. A rebreathing bag attached to the anesthetic system permits manual control if desired. The unit weighs 13 lb. and can be attached to any standard anesthetic machine or mounted in an anesthetic cylinder yoke.
PRODUCER: Manufactured by the J. J. Monaghan Company, Denver. Distributed by the National Cylinder Gas Division of Chemetron Corporation, Chicago.

• RACOBALAMIN®-57

DESCRIPTION: For use in diagnosing pernicious anemia by the Schilling test, Racobalamin (Co^{57}-labeled vitamin B_{12}) is available in solution or capsule form. The patient is given 0.5 μc Racobalamin, which is followed in two hours by 1 mg. BEVIDOX® solution. The test procedure is carried out on urine collected over the next 24 hours. A diagnostic anemia kit is available which contains 5 capsules Racobalamin, 1 vial Bevidox solution, and 2 capsules intrinsic factor concentrate.
PRODUCER: Abbott Laboratories, North Chicago. (Manufactured at Radio-Pharmaceutical Laboratories, Oak Ridge, Tenn.)

• BALVIS

PURPOSE: To treat peptic ulcer and relieve gastric hyperacidity accompanying gastritis.
COMPOSITION: Each tablet contains:

Guar cellupectinoid	275 mg.
Magnesium oxide	70 mg.
Aluminum hydroxide gel	80 mg.
Magnesium trisilicate	160 mg.

DOSAGE AND ADMINISTRATION: For peptic ulcer, 2 tablets initially every two to four hours until relief is obtained. For maintenance therapy in managing hyperacidity, 1 or 2 tablets four times a day or as needed. The tablets are not to be chewed.
HOW SUPPLIED: Packages of 40 and 100.
PRODUCER: G. W. Carnrick Company, Newark, N. J.

(Continued on page A-102)

asleep minutes after

This is the promise of Noludar 300... a night of deep, refreshing sleep without risk of habituation or toxicity... 6 to 8 hours of undisturbed rest... an easy awakening in the morning, free of fogginess or barbiturate "hangover." Try Noludar 300 for your next patient with a sleep problem. One capsule at bedtime. Chances are she'll tell you

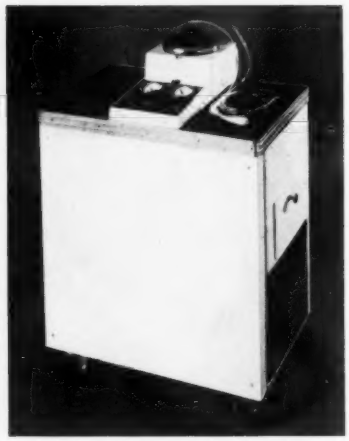
"I slept like a log"

NOLUDAR® 300

brand of methyprylon

300-mg capsules

ROCHE LABORATORIES • Division of Hoffmann-La Roche Inc • Nutley 10, New Jersey



• GASTRIC HYPOTHERMIA MACHINE

DESCRIPTION: Used to treat massive upper gastrointestinal hemorrhage by producing local gastric hypothermia, this mobile machine includes a ⅓ H.P. sealed refrigeration unit, a reservoir with a capacity of approximately 1 gal., and a ⅙ H.P. centrifugal water pump. Flexible lines are used throughout the liquid system to eliminate vibration and breakage. A plastic catheter, with an outside diameter equivalent to a No. 18 French nasogastric tube, and a No. 260 polyethylene catheter can be used as the outer outflow and inflow tubes, respectively. A thin-walled, elongated latex balloon is used to receive the cooling fluid. The cabinet is constructed of 20 gauge steel and has a finish of baked enamel and a FORMICA® top. The machine operates on a 110 V, 60 cycle AC current, and is 27 in. wide, 18 in. deep and 33½ in. high.
PRODUCER: Swenko Manufacturing Company, Minneapolis.

• SUPER-EDISONITE

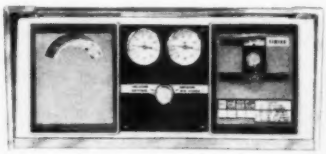
DESCRIPTION: For cleaning surgical instruments and glassware, this powder may be safely used on a wide variety of materials. The high-potency formula eliminates the need for separate soaking solutions, and the pH of 8.0 permits efficient cleaning without tarnishing or corroding. This product is available in 1 lb. and in 3 lb. 2 oz. packages, making 64 gal. and 200 gal. of solution, respectively.
PRODUCER: S. M. Edison Chemical Co., Inc., Chicago.

• PROBITAL®

PURPOSE: Gastrointestinal antispasmodic therapy.
COMPOSITION: Each tablet contains 7.5 mg. propantheline bromide and 15 mg. phenobarbital.
INDICATIONS FOR USE: Functional gastrointestinal disorders, pylorospasm, gastritis, biliary dyskinesia, colic spasm and diverticulitis.
DOSAGE AND ADMINISTRATION: 1 tablet at mealtime and 1 at bedtime. Dosage may be increased if necessary.
HOW SUPPLIED: Bottles of 100 and 500.
PRODUCER: G. D. Searle & Co., Chicago.

• BROMSULPHALEIN®
(New Package Form)

DESCRIPTION: Bromsulphalein is now supplied in easily opened 3 cc., 7.5 cc. and 10 cc. glass ampules.
PRODUCER: Hynson, Westcott & Dunning, Inc., Baltimore.



• STEAM STERILIZER CONTROL SYSTEM

DESCRIPTION: Employing an oil-sealed, high-vacuum pump, this unit sterilizes and dries a load of dry goods in approximately 15 minutes. An automatic time-temperature integrator determines exposure time based on the sterilizing temperature attained. Following the postvacuum phase, during which the chamber pressure is rapidly lowered, sterilized dressings are removed completely dry. An automatic absolute-pressure switch provides for correct pressures regardless of barometric changes, and a monitor indicates whether or not the correct temperature has been maintained throughout the cycle. The system can be operated manually in the event of power failure. Console construction allows the unit to be easily serviced and provides for its use with new or converted sterilizing equipment. A recording two pen gauge showing temperature and pressure is optional.
PRODUCER: Wilmot Castle Co., Rochester, N. Y.

(Continued on page A-104)

Metamine®
(trolnitrate phosphate, Leeming, 10 mg.)
Sustained

in coronary insufficiency

helps you dilate the coronaries

In pharmacologic studies at Pasteur Institute and McGill University, the vasodilator activity of trolnitrate phosphate (METAMINE) was found to be equal or superior to that of nitroglycerin, and of much longer duration.[1-2]

In coronary insufficiency, one METAMINE SUSTAINED tablet q. 12 h. markedly reduces the number and severity of anginal attacks and increases exercise tolerance, with virtual freedom from nitrate side effects and less danger of a forgotten dose.[3-4] Bottles of 50 and 500 tablets.

Thos. Leeming & Co. Inc.
New York 17, N. Y.

1. Bovet, D., and Nitti-Bovet, F.: Arch. Internat. de pharmacodyn. et therap. 83:367, 1946. 2. Melville, K.I., and Lu, F.C.: Canad. M.A.J. 65:11, 1951. 3. Fuller, H.L. and Kassel, L.E.: Antibiotic Med. & Clin. Therapy 3:322, 1956. 4. Eisfelder, H.W. et al.: J. Am. Geriatrics Soc. 8:62, 1960.

1 tablet all day

1 tablet all night

• SAFETRODE®

DESCRIPTION: Developed to eliminate burns resulting from the improper use of metallic indifferent electrode plates in electrosurgery, this large, flat condenser (25½ by 15½ in.) is molded in autoclavable neoprene and will fit any electrosurgical unit. It is placed on the operating table in a position which approximates the trunk of the body, and a sterile sheet is draped over it. The patient can be moved to any position. When in use the Safetrode matches the capacity of the patient's body and induces energy into the patient.
PRODUCER: The Birtcher Corp., Los Angeles.

• CRYSTALLINE GLUCAGON HYDROCHLORIDE

PURPOSE: To treat hypoglycemic reactions in diabetic patients and to terminate therapeutic insulin coma in psychiatric patients.
DOSAGE AND ADMINISTRATION: For diabetic patients with hypoglycemia, the usual dose is 0.5 to 1 mg. administered parenterally. Additional doses may be given if the patient is not awake in 20 minutes. If the patient fails to respond to repeated injections of glucagon hydrochloride, glucose must be given intravenously. For psychiatric patients in an insulin coma, the usual dose is 0.5 to 1 mg. administered parenterally. Doses of 2 mg. or more are needed to terminate the later stages of coma. Additional doses may be given if the patient is not awake in 20 minutes.
HOW SUPPLIED: 1 and 10 mg. ampules of dry powder, with 1 and 10 cc. ampules of diluting solution (1.6 per cent glycerin and 0.2 per cent phenol), respectively.
PRODUCER: Eli Lilly and Company, Indianapolis.

• DOMOFORM®

DESCRIPTION: Providing antibacterial and antifungous action in treatment of infectious and eczematous skin conditions, this agent contains 3 per cent iodochlorhydroxyquin in the ACID MANTLE® vehicle (creme) or in the DOMOLENE® base (ointment). Either preparation may be applied as often as necessary.

Other dermatologic agents recently released by the same company include Domoform-HC, Domoform-HC Forte, Domolene-HC and LIDAMYCIN® Creme.
PRODUCER: Dome Chemicals Inc., New York.

• CARDIOQUIN® TABLETS

PURPOSE: To treat cardiac arrhythmias.
COMPOSITION: Each tablet contains 275 mg. quinidine polygalacturonate (equivalent to 200 mg. quinidine sulfate).
DOSAGE AND ADMINISTRATION: Dosage must be individualized according to patient's needs. Cardioquin may be used in any regimen being employed for quinidine sulfate on a dose-for-dose basis.
PRODUCER: The Purdue Frederick Company, New York and Toronto.

• CROUPAIRE HUMIDIFIER

DESCRIPTION: Designed to deliver cool vapor directly to the patient, this humidifier provides continuous therapeutic permeation and moistening of the upper respiratory tract. The minute water particles in the vapor do not dampen bedclothes or furniture. Weighing 6 lb., the humidifier occupies a table space of 14 by 7½ in. and may be plugged into any AC outlet. The 2½ qt. water reservoir allows operation of the Croupaire for 10 hours without refilling.
PRODUCER: Air-Shields, Inc., Hatboro, Pa.

There's hardly ever a case who can't tolerate BENTYL

(dicyclomine) hydrochloride

97%

well tolerated[1-8]

(even in glaucoma patients)

The use of BENTYL in glaucoma patients is an unusual index of its safety.[9-11] Because of highly selective action on the G.I. tract, blurred vision, dry mouth or urinary retention rarely occur.

Usual dosage: 20 mg. t.i.d. You may prescribe BENTYL in any of 7 convenient dosage forms. There is a BENTYL dosage form to suit every age group and therapeutic need. See Page 743, Physicians' Desk Reference, 1960.

17. Lorber, S. H., and Shay, H.: Fed. Proc. *12*:90, 1953. 18. Johnston, R. I.: J. Indiana M. A. *46*:869, 1953. 19. Marien, B., Webster, D. R., and Tidmarsh, C. J.: Gastroenterology *24*:200, 1953. 20. Hardin, J. H., Levy, J. S., and Seager, L.: South. M. J. *47*:1190, 1954. 21. Sleisenger, M. H., Eisenbud, M., and Almy, T. P.: Gastroenterology *27*:829, 1954. 22. Weiss, S.: Am. J. Gastroenterology *23*:69 (Editorial) 1955. 23. Illingworth, R. S.: Lancet *2*:1119, 1959. 24. McHardy, G. G., and Browne, D. C.: South. M. J. *45*:1139, 1952. 25. Miller, B. N.: J. South Carolina, M. A. *48*:1, 1952.

Merrell

THE WM. S. MERRELL COMPANY • CINCINNATI, OHIO • ST. THOMAS, ONTARIO

THE MEDICAL *Bookman*

► THE YEAR BOOK OF GENERAL SURGERY (1960-1961)

Edited by Michael E. DeBakey, M.D., Professor of Surgery and Chairman, Cora and Webb Mading Department of Surgery, Baylor University College of Medicine, Houston. 616 pages, illustrated. 1960, The Year Book Publishers, Inc., Chicago. $8.00.

Probably the most rapid way to review the recent significant contributions to general surgery and to anesthesiology is to read this volume, which contains abstracts of articles published primarily in American surgical journals. The bulk of the text is divided equally between thoracic surgery, including the cardiovascular system, and abdominal surgery.

It is immediately apparent that the greatest amount of surgical activity and progress is in the thoracic and cardiovascular areas. Considerable time and energy are being expended in the treatment of cancer, but progress is slow. Interest is high in regional perfusion of the body with chemotherapeutic agents and in the investigations of cancer and immunology.

In the cardiovascular field, new reports deal with the extension of surgery to the peripheral vessels, including the cerebral and renal arteries, and with clarification of problems associated with both hypothermia and cardiopulmonary bypass procedures.

The section on abdominal surgery consists mostly of case reports and studies of common problems, such as peptic ulcer, cancer, pancreatitis, biliary tract diseases, nutrition, intestinal obstruction, inflammatory and congenital lesions of the intestinal tract, and various types of hernia. Results of experimental studies relating to the gastrointestinal tract are also included.

Many new problems are covered in the section on anesthesia and respiration. Among the topics discussed are experiences with new muscle relaxants, poor-risk patients, and anesthetic problems associated with new cardiopulmonary operative procedures.

The abstracts are supplemented with reproductions of photographs and tables from the original articles. An author index and a subject index increase the usefulness of this book.

Y. S.

► LETTERS TO MY SON

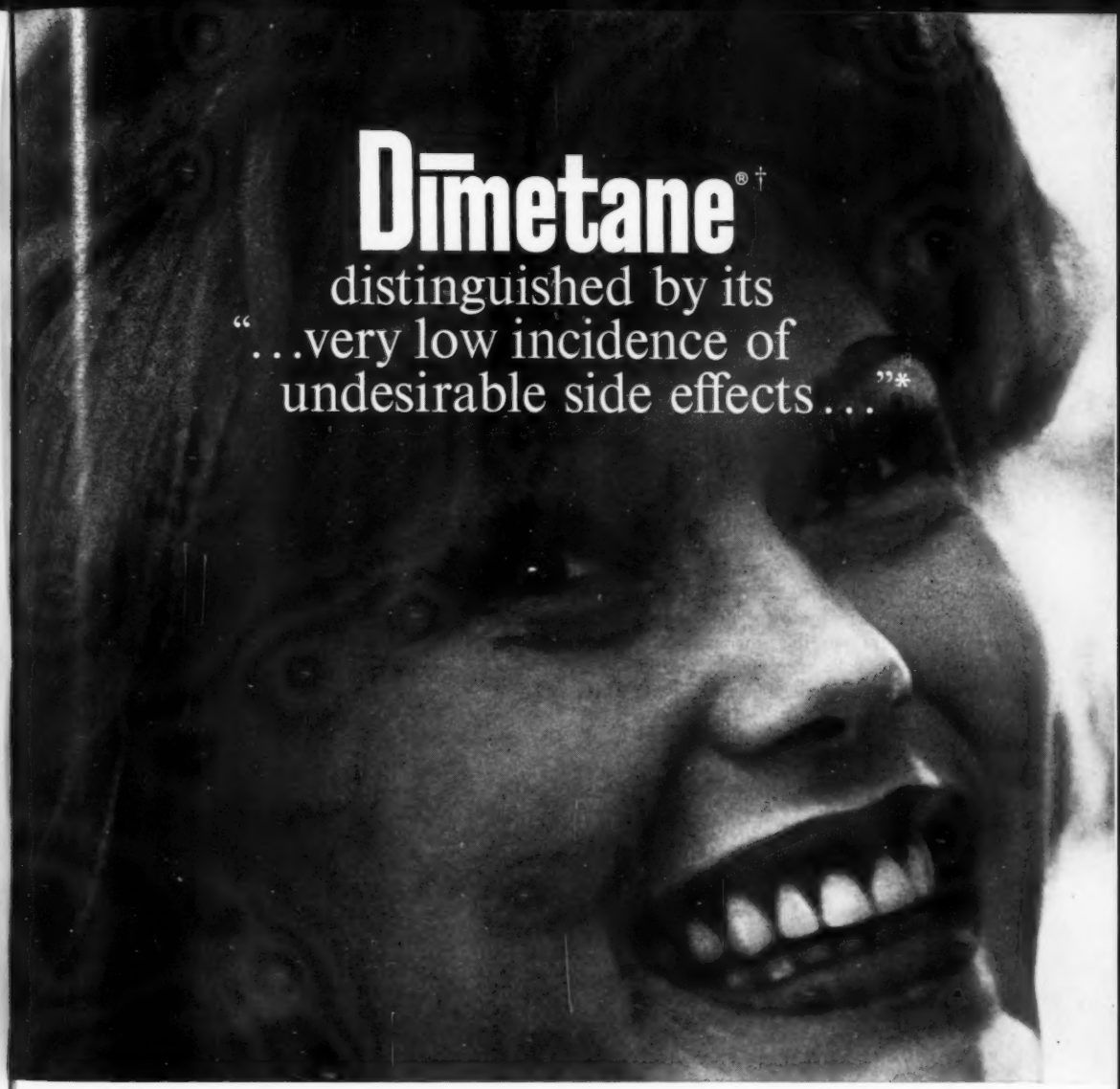
By Wendell J. S. Krieg, Ph.D., Professor of Anatomy, Northwestern University Medical School, Chicago. Originally published serially in POSTGRADUATE MEDICINE. *82 pages. 1960, Brain Books, Evanston, Illinois. $3.00.*

Dr. Krieg has produced some wonderful bits of wise advice in this book, which is comprised of 12 letters written by a father (Dr. Krieg) to his son (anyone reading this book). In my mind it represents the deep thoughts and feelings of a wonderful scholar, teacher and gentleman.

I do hope that all physicians will read this small and inexpensive book. It should be "must" reading for all medical and science students.

I. P. F.

(Continued on page A-140)



even in allergic infants

FROM A CLINICAL STUDY* IN ANNALS OF ALLERGY

Patients	200 infants and children, ages 2 months to 14 years
Diagnosis	Perennial allergic rhinitis
Therapy	Dimetane Elixir
Results	in 149, *good* results / in 40, *fair* results
Side Effects	Encountered in *only* 7 patients (in all except one, the side effect was mild drowsiness)

In allergic patients *of all ages,* Dimetane has been shown to work with an effectiveness rate of about 90% and to produce an exceptionally low incidence of side effects. Complete clinical data are available on request to the Medical Department. *Supplied:* DIMETANE Extentabs® (12 mg.), Tablets (4 mg.), Elixir (2 mg./5 cc.), new DIMETANE-TEN Injectable (10 mg./cc.) or new DIMETANE-100 Injectable (100 mg./cc.).

Robins

*MC GOVERN, J. P., MC ELHENNEY, T. R., HALL, T. R., AND BURDOM, K.D.: ANNALS OF ALLERGY 17:918, 1959.

A. H. ROBINS CO., INC., RICHMOND 20, VIRGINIA / ETHICAL PHARMACEUTICALS OF MERIT SINCE 1878

† PARABROMDYLAMINE MALEATE

► SYNOPSIS OF PATHOLOGY

By W. A. D. Anderson, M.D., Professor of Pathology, University of Miami School of Medicine, Coral Gables, Florida. Ed. 5. 876 pages with 414 illustrations and four color plates. 1960, The C. V. Mosby Company, St. Louis. $9.25.

In this new edition of a work which has become a medical classic, the author has recognized the problem of the struggle between comprehensiveness and completeness on one hand and the practicality of publication space on the other. The text covers many conditions that have come to light since the earlier editions were published, yet, because of its size, the book retains its recognized usefulness as a synopsis.

As in previous editions, many illustrations of well-selected subjects have been included to assist the reader where words have had to be restricted. Several specific illustrations could be improved technically, however, and it is hoped that the author will consider this in any future editions.

J. E. E.

► CURRENT SURGICAL MANAGEMENT II
A Book of Alternative Viewpoints on Controversial Surgical Problems

Edited by John H. Mulholland, M.D., New York University School of Medicine, New York, Edwin H. Ellison, M.D., Marquette University School of Medicine, Milwaukee, and Stanley R. Friesen, M.D., University of Kansas Medical Center, Kansas City, with 50 contributors. 348 pages, illustrated. 1960, W. B. Saunders Company, Philadelphia and London. $8.00.

In this stimulating and thought-provoking book, the contributors expand on the controversial and usually newer aspects of surgical treatment. Some directly opposite viewpoints are presented and substantiated by reviews of results obtained in series of patients.

The abdominal surgical problems covered include duodenal ulcer, polyps of the colon, hiatal hernia, carcinoma of the pancreas, conditions in the biliary tract, intestinal obstruction, and rectal prolapse. Other discussions are concerned with carcinoma of the breast, peripheral arterial surgery, thromboembolization, and renal failure.

All the contributors are nationally known surgeons whose works have been published previously, but in many instances in this book they have taken definite stands and at times have analytically criticized the viewpoints expressed by others. Among some points of practical interest to the surgeon are the pros and cons on the repair of common duct stricture by choledochojejunostomy or by end-to-end duct anastomosis, the choice of treatment for breast carcinoma, the question of the need for intestinal antibiotics, and how radical the management of colonic polyps should be.

This book differs from a textbook in that selected subjects are covered, and at times opposing theories are presented side by side, so that the reader must decide for himself which school of thought is correct. More often than not, both theories have well-chosen points which may be applied to individual cases.

Y. S.

► SHAW'S TEXTBOOK OF OPERATIVE GYNAECOLOGY

Revised by John Howkins, M.D., Obstetrical and Gynaecological Surgeon, St. Bartholomew's Hospital, London. Ed. 2. 484 pages, illustrated. 1960, The Williams & Wilkins Company, Baltimore. $20.00.

Profusely illustrated with both black-and-white and color prints, this textbook of gynecologic surgery emphasizes the orthodox and accepted British practice and will serve as a guide to the apprentice surgeon in performing gynecologic operations. In conjunction with surgical technics, the author discusses preoperative preparation as well as postoperative treatment and complications. A chapter also is devoted to nongynecologic conditions which might be found at the time of surgery. For those particularly interested in the treatment of cervical or uterine malignancies, a discussion of radiation therapy is likewise included.

As a fitting conclusion to any text on abdominal surgery, the author discusses the diagnosis and treatment of cardiac arrest. Particular reference throughout the book to the anatomy involved will be appreciated by the physician who performs occasional surgery, while the specialist will find additional references to the treatment of the pathologic condition at the conclusion of each chapter.

E. A. B.

(Continued on page A-143)

▶ THE YEAR BOOK OF OBSTETRICS AND GYNECOLOGY (1960-1961)

Edited by J. P. Greenhill, M.D., Senior Attending Obstetrician and Gynecologist, Michael Reese Hospital, Chicago. 576 pages, illustrated. 1960, The Year Book Publishers, Inc., Chicago. $8.00.

As in previous years, this volume presents in abstract form much of the literature pertinent to obstetrics and gynecology which has been published during the preceding year. As an adjunct to this edition, the authors have included material relevant to the newborn.

The book is an excellent reference text and will be of great use to practitioners who do not have ready access to medical libraries.

E. A. B.

Books received are acknowledged in this department. As space permits, books of principal interest to our readers are reviewed more extensively.

Clinical Vectorcardiography and Electrocardiography. By Edward Massie, M.D., Associate Professor of Clinical Medicine, and Thomas J. Walsh, M.D., Instructor of Clinical Medicine, Washington University School of Medicine, St. Louis. 592 pages, illustrated. 1960, The Year Book Publishers, Inc., Chicago. $27.50.

Motor Examination of Peripheral Nerve Injuries. By Y. T. Oester, M.D., Professor of Pharmacology, Stritch School of Medicine of Loyola University, Chicago, and John H. Mayer, Jr., M.D., Percy Jones General Hospital, Battle Creek, Michigan. 89 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $5.50.

Annals of the New York Academy of Sciences, 1960. Deuterium Isotope Effects in Chemistry and Biology. Vol. 84, Art. 16. 208 pages, illustrated. $4.00.

Clinical Cardiopulmonary Physiology. Sponsored by the American College of Chest Physicians. Edited by Burgess L. Gordon, M.D., Ross C. Kory, M.D., Albert H. Andrews, Jr., M.D., John F. Briggs, M.D., Benjamin M. Gasul, M.D., Edwin R. Levine, M.D. and John J. Sampson, M.D., with 92 contributors. Ed. 2. 1,001 pages, illustrated. 1960, Grune & Stratton, Inc., New York and London. $28.50.

The Management of Fractures and Soft Tissue Injuries. By the Committee on Trauma, American College of Surgeons. 372 pages, illustrated. 1960, W. B. Saunders Company, Philadelphia and London. $5.00.

Diverticulitis. Modern Medical Monographs. By Sara M. Jordan, M.D., New England Baptist Hospital, and Russell S. Boles, M.D., Department of Gastroenterology, Lahey Clinic, Boston. 90 pages, illustrated. 1960, Grune & Stratton Inc., New York and London. $4.75.

Blood Diseases of Infancy and Childhood. By Carl H. Smith, M.D., Professor of Clinical Pediatrics, Cornell University Medical College, New York. 572 pages, illustrated. 1960, The C. V. Mosby Company, St. Louis. $17.00.

A System of Medical Hypnosis. By Ainslie Meares, M.D., President, International Society for Clinical and Experimental Hypnosis. 484 pages. 1960, W. B. Saunders Company, Philadelphia and London. $10.00.

The Commonsense Book of Drinking. By Leon D. Adams. 210 pages. 1960, David McKay Company, Inc., New York. $3.95.

Regulation of the Inorganic Ion Content of Cells. Ciba Foundation Study Group. Edited by G. E. W. Wolstenholme, O.B.E. and Cecilia M. O'Connor, B.Sc. 100 pages with 16 illustrations. 1960, Little, Brown & Company, Boston.

Radiation Therapy of Early Prostatic Cancer. American Lecture Series. By R. H. Flocks, M.D. and D. A. Culp, M.D., Department of Urology, State University of Iowa College of Medicine, Iowa City. 73 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $4.50.

Clinicopathological Conferences of the Massachusetts General Hospital. Edited by Benjamin Castleman, M.D., Chief, James Homer Wright Pathology Laboratories, and H. Robert Dudley, Jr., M.D., Assistant in Pathology, Massachusetts General Hospital, Boston. 295 pages, illustrated. 1960, Little, Brown & Company, Boston and Toronto. $12.50.

Resuscitation of the Newborn Infant; Principles and Practice. Edited by Harold Abramson, M.D., Professor of Clinical Pediatrics, New York Medical College, New York, with 24 contributors. 274 pages with 36 illustrations. 1960, The C. V. Mosby Company, St. Louis. $10.00.

Progress in the Treatment of Fractures and Dislocations (1950-1960). By Thomas B. Quigley, M.D., Assistant Clinical Professor of Surgery, and Henry Banks, M.D., Clinical Associate in Orthopedic Surgery, Harvard Medical School, Boston. 102 pages. 1960, W. B. Saunders Company, Philadelphia and London. $2.50.

Leukemia Cutis. American Lecture Series. By Samuel M. Bluefarb, M.D., Associate Professor of Dermatology, Northwestern University Medical School, Chicago. 489 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $18.50.

Advances in Internal Medicine. Edited by William Dock, M.D., State University of New York College of Medicine at New York City, and I. Snapper, M.D., Beth-El Hospital, Brooklyn. Vol. 10. 390 pages, illustrated. 1960, The Year Book Publishers, Inc., Chicago. $10.50.

Disc Lesions and Other Intervertebral Derangements. Treated by manipulation, traction and other conservative methods. By E. J. Crisp, M.D., Consultant Physician Emeritus in Physical Medicine, Guy's Hospital, London. 158 pages, illustrated. 1960, E. & S. Livingstone Ltd., Edinburgh and London. Distributed by The Williams & Wilkins Company, Baltimore. $3.75.

serenity without somnolence

with sharpened mental acuity and restoration of normal drive

References: 1. Carsley, S. H., and Olson, J. A.: Submitted for publication. 2. Ayd, F. J.: Current Therap. Res. 1:41, 1959. Additional bibliography: Ernst, E. Clin. Med. 7:1349, 1960. Bodi, T., et al.: Clin. Res. 8:72, 1960. Dunlop, E.: Submitted for publication. Grimaldi, R.: Presented at the Annual Congress Pan American Medical Association, May 6, 1960, Mexico City. Compilation of case reports received by the Medical Department, White Laboratories.

to replace or reduce insulin dosage

to ensure control where diet alone has failed

to realize the full potential of oral therapy

IN BRIEF

DIABINESE, a potent sulfonylurea, provides smooth, long-lasting control of blood sugar permitting economy and simplicity of low, once-a-day dosage. Moreover, DIABINESE often works where other agents have failed to give satisfactory control.

INDICATIONS: Uncomplicated diabetes mellitus of stable, mild or moderately severe nonketotic, maturity-onset type. Certain "brittle" patients may be helped to smoother control with reduced insulin requirements.

ADMINISTRATION AND DOSAGE: Familiarity with criteria for patient selection, continued close medical supervision, and observance by the patient of good dietary and hygienic habits are essential.

Like insulin, DIABINESE dosage must be regulated to individual patient requirements. Average maintenance dosage is 100-500 mg. daily. For most patients the recommended starting dose is 250 mg. given once daily. Geriatric patients should be started on 100-125 mg. daily. A priming dose is not necessary and should not be used; most patients should be maintained on 500 mg. or less daily. Maintenance dosage above 750 mg. should be avoided. Before initiating therapy, consult complete dosage information.

SIDE EFFECTS: In the main, side effects, e.g., hypoglycemia, gastrointestinal intolerance, and neurologic reactions, are related to dosage. They are not encountered frequently on presently recommended low dosage. There have been, however, occasional cases of jaundice and skin eruptions primarily due to drug sensitivity; other side effects which may be idiosyncratic are occasional diarrhea (sometimes sanguineous) and hematologic reactions. Since sensitivity reactions usually occur within the first six weeks of therapy, a time when the patient is under very close supervision, they may be readily detected. Should sensitivity reactions be detected, DIABINESE should be discontinued.

PRECAUTIONS AND CONTRAINDICATIONS: If hypoglycemia is encountered, the patient must be observed and treated continuously as necessary, usually 3-5 days, since DIABINESE is not significantly metabolized and is excreted slowly. DIABINESE as the sole agent is not indicated in juvenile diabetes mellitus and unstable or severely "brittle" diabetes mellitus of the adult type. Contraindicated in patients with hepatic dysfunction and in diabetes complicated by ketosis, acidosis, diabetic coma, fever, severe trauma, gangrene, Raynaud's disease, or severe impairment of renal or thyroid function. DIABINESE may prolong the activity of barbiturates. An effect like that of disulfiram has been noted when patients on DIABINESE drink alcoholic beverages.

SUPPLIED: As 100 mg. and 250 mg. scored chlorpropamide tablets.

More detailed professional information available on request.

Science for the world's well-being™ Pfizer

PFIZER LABORATORIES
Division, Chas. Pfizer & Co., Inc. Brooklyn 6, New York

Great Names in American Medical History

THE names of many physicians loom large in the history of medicine. Some have gained repute through notable discoveries which followed investigations. Others have been educators who raised the standards of medical education. Some achieved fame through political distinction. Others are known by the monuments erected to them by grateful patients. Sometimes a physician has pioneered the opening up of areas of land which previously were parts of the wilderness. Moreover, an occasional name appears such as that of the famous John Evans of Illinois and Colorado, who founded two universities and became the governor of Colorado and whose name is now borne by a mountain.

The names and achievements of great men are an inspiration. Young men, hearing what these men have accomplished, are inspired to greater individual efforts. This thought has perhaps never been better expressed than in the stanza of Longfellow's trite poem, "A Psalm of Life," which reads,

> Lives of great men oft remind us
> We can make our lives sublime,
> And, departing, leave behind us
> Footprints on the sands of time;

Stimulated by these thoughts, POSTGRADUATE MEDICINE undertook a project of which the initial result appears on the following page. A letter was written to the president or executive secretary of each of the 50 state medical societies with a request that a responsible official or board or a specially appointed committee select the name of the most distinguished physician in that state. The only stipulation was that the physician nominated for this distinction should not be living, notwithstanding the possibility that some physician still active might have achieved greater distinction than any in the state who had gone before.

Obviously, such a decision in some of the older states would be exceedingly difficult because of the great number of names that comes to mind, particularly in making a choice of distinction in some of the various fields that have already been mentioned. Indeed, the responses from some of the states mention two or more great names. In preparing this feature, therefore, in some instances several names may be mentioned as representing the greatest names in medicine in the state concerned.

The biographies, which will appear monthly, will not be published in alphabetical order by states, since a few states still have the subject under consideration by boards or committees. Fortunately, however, the state of Alabama unanimously selected the name of William Crawford Gorgas as the most distinguished physician in Alabama, and the series will begin with his sketch.

Great Names in American Medical History

Alabama

William Crawford Gorgas, M.D.

THE public relations committee of the medical association of the state of Alabama responded to the request for the name of Alabama's most distinguished physician with unanimous agreement on the name of William Crawford Gorgas (1854-1920). Among other names mentioned were J. Marion Sims, John Wyeth, James S. McLester and Seale Harris.

William Crawford Gorgas was born in Touminville, Alabama, in 1854. His father was a general in the Confederate Army, achieving that rank after graduation from the United States Military Academy at West Point. William Gorgas failed repeatedly to secure an appointment to West Point and began the study of medicine at Bellevue Hospital Medical College in New York. After graduation he entered the United States Army Medical Service in 1880. In 1898 he went to Havana to stamp out an epidemic of yellow fever. Convinced by the work of Reed's Yellow Fever Commission, he carried out a thorough campaign of mosquito extermination. In three months Havana became free of this disease for the first time in its history.

In 1904 Gorgas was sent by President Theodore Roosevelt to the Canal Zone. Without Gorgas' ability as a sanitarian to free the canal of yellow fever and other infections, General George Goethals would have failed in his construction of the Panama Canal. Panama, once known as the "White Man's Grave," is now recognized as one of the healthiest communities in the world. Gorgas' distinction caused him to be called by other nations, so that he worked in Johannesburg, South Africa, to control epidemic pneumonia among the native miners, and he surveyed yellow fever in South America for the Rockefeller Foundation.

In 1914 Gorgas became the surgeon general of the United States Army, achieving great distinction in this position in World War I.

You see an improvement within a few days
Thanks to your prompt treatment and the smooth action of Deprol, her depression is relieved and her anxiety and tension calmed – *often in a few days.* She eats well, sleeps well and soon returns to her normal activities.

Lifts depression...as it calms anxiety!

Smooth, balanced action lifts depression as it calms anxiety...rapidly and safely

Balances the mood – no "seesaw" effect of amphetamine-barbiturates and energizers. While amphetamines and energizers may stimulate the patient – *they often aggravate anxiety and tension.*

And although amphetamine-barbiturate combinations may counteract excessive stimulation – *they often deepen depression.*

In contrast to such "seesaw" effects, Deprol's smooth, *balanced* action lifts depression as it calms anxiety – both at the same time.

Acts swiftly – the patient often feels better, sleeps better, within a few days. Unlike the delayed action of most other antidepressant drugs, which may take two to six weeks to bring results, Deprol relieves the patient quickly – often within a few days. Thus, the expense to the patient of long-term drug therapy can be avoided.

Acts safely – no danger of liver damage. Deprol does not produce liver damage, hypotension, psychotic reactions or changes in sexual function – frequently reported with other antidepressant drugs.

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this dose may be gradually increased up to 3 tablets q.i.d.

Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate. **Supplied:** Bottles of 50 light-pink, scored tablets. Write for literature and samples.

Deprol®

WALLACE LABORATORIES / *Cranbury, N. J.*

69-2125

CONSISTENT RESPONSE
IN VAGINAL INFECTIONS

ANTIBACTERIAL, ANTIMONILIAL, ANTITRICHOMONAL EFFECTS—OPTIMAL DISPERSION, PROLONGED RETENTION

85% SUCCESS:[1,2] TRIBURON CHLORIDE—THE CLINICALLY PROVEN MICROBICIDE—PROVIDES RAPID SYMPTOMATIC RELIEF AS WELL AS MICROBICIDAL CONTROL OF TRICHOMONAL, MONILIAL AND NONSPECIFIC VAGINITIS. IN ONE STUDY, DISCHARGE, ITCHING AND BURNING DISAPPEARED IN 67 OF 73 WOMEN AFTER ONLY 3 OR 4 APPLICATIONS; AFTER TWO WEEKS, CULTURES WERE NEGATIVE IN 61 PATIENTS. SIMILAR RESULTS WERE NOTED IN ANOTHER SERIES OF 55 WOMEN.[2]

NOW AVAILABLE IN TWO FORMS

NEW TRIB VAGINAL SUPPOSITORIES PROVIDE THE EFFICACY OF TRIBURON CHLORIDE IN A WATER-SOLUBLE, SELF-EMULSIFYING BASE THAT ENHANCES DISPERSION AND PROLONGS THERAPEUTIC EFFECTS, EVEN IN THE PRESENCE OF PROFUSE DISCHARGE. TRIB VAGINAL SUPPOSITORIES ARE PROVIDED WITH REUSABLE PLASTIC APPLICATORS.

WIDELY ACCEPTED TRIBURON VAGINAL CREAM—SMOOTH, WHITE, NONSTAINING, VIRTUALLY NONIRRITATING TO THE VAGINAL MUCOSA, WITH NO HINT OF MEDICINAL ODOR. DISPOSABLE APPLICATORS ARE SUPPLIED WITH THE CREAM.

INDICATIONS: TRIB VAGINAL SUPPOSITORIES AND TRIBURON VAGINAL CREAM FOR VULVITIS AND VAGINITIS DUE TO *TRICHOMONAS VAGINALIS*, *CANDIDA ALBICANS*, *HEMOPHILUS VAGINALIS* AS WELL AS MIXED INFECTIONS; AFTER CAUTERIZATION, CONIZATION AND IRRADIATION; FOR SURGICAL AND POSTPARTUM TREATMENT. THERAPY MAY BE CONTINUED DURING PREGNANCY AND MENSTRUATION.

SUPPLIED: TRIB VAGINAL SUPPOSITORIES—BOXES OF 24, WITH REUSABLE APPLICATOR. TRIBURON VAGINAL CREAM—3-OUNCE TUBES WITH 18 DISPOSABLE APPLICATORS. CONSULT LITERATURE FOR DOSAGE REQUIREMENTS, AVAILABLE ON REQUEST, BEFORE PRESCRIBING.

REFERENCES: 1. N. MULLA AND J. J. McDONOUGH, *ANN. NEW YORK ACAD. SC.*, 82:(ART. 1), 182, 1959. 2. L. E. SAVEL, D. B. GERSHENFELD, J. FINKEL AND P. DRUCKER, *IBID.*, P. 186.

ROCHE LABORATORIES · DIVISION OF HOFFMANN-LA ROCHE INC · NUTLEY 10, N. J.

NEW Trib™ Vaginal Cream & Suppositories

contains Triburon Chloride 0.1%

FORMERLY TRIBURON VAGINAL CREAM

decisive microbicidal therapy in a delicate matter

not an antibiotic · not a nitrofuran

ROCHE LABORATORIES · DIVISION OF HOFFMANN-LA ROCHE INC · NUTLEY 10, N. J.

DR. Pepys' Pages

Personal Diary
and Observations on
Medical Life
by MORRIS FISHBEIN, M.D.

Dec. 1—To the University of Chicago Cancer Research Foundation meeting, where Dr. Wright Adams was elected president, and Dr. H. Stanley Bennett, dean of the Division of the Biological Sciences, coming from Oregon, spoke beautifully of opportunities in medicine and particularly in the field of research on cancer.

Dec. 2—At noon to the Illinois Athletic Club at the request of John Egdorf of the Municipal Tuberculosis Sanitarium. Here were representatives of all the Chicago agencies which deal particularly with tuberculosis, and we discussed the implementation of the conclusions of the Arden House Conference.

Dec. 3—Early to the airport to meet Professor Ernst Chain, who flew in from Italy. To a luncheon at the Ambassador with Irv Kupcinet, Dr. Chain and Louis Zahn, the purveyor of pharmaceuticals. In the afternoon came Paul Wermer, and with him and Dr. Chain to the Standard Club to dine and then to hear the opera "Simon Boccanegra." Thereafter to sit from midnight until 4 A.M. on Kupcinet's TV program "At Random," and here also were author Robert St. John; a believer in flying saucers named Williamson, who is an anthropologist and archaeologist as well; comedians Bert Lahr and Herb Shriner; the poet Howard Nemerov; and the author of the life of Martin Luther King, Mr. Reddick of Baltimore.

Dec. 4—After a cocktail party in the Ambassador's Sarah Siddons' room, to a dinner in the Guildhall for the awarding of citations to Ernst Chain, Bela Schick and Ben Gasul. The awards were conferred by R. W. Harrison of the University of Chicago, Willis Potts and Sam Andelman, with old Pepys as the toastmaster.

Dec. 5—In the afternoon Mistress Pepys gave a reception honoring Dr. Chain, and here came all the deans of the medical schools, the biochemists of the universities and of the Cook County Hospital, and many other friends to greet our distinguished guest. Thereafter to the Civic Opera House, where a great audience came to benefit the University of Chicago Cancer Foundation and to hear Harry Belafonte in a concert full of excitement and interest. Then to the Ambassador for a reception for Belafonte, and he was most charming, signing a record for the Nobel prize winner Chain and then requesting his autograph as something worth treasuring.

Dec. 6—To the University of Chicago to hear Dr. Chain lecture on his new work with fermentation processes. In the evening to dine with Mayor Daley, Pat Hoy and Strohl, who entertained for the Advisory Board of the Municipal Tuberculosis Sanitarium of Chicago.

Dec. 7—Early to New York and for luncheon with Ted Gotthelf and then to tape an interview on new advances in biochemistry for "The Voice of Medicine."

Dec. 8—Early with Bill Lasdon to Morris Plains, and then to luncheon with Elmer Bobst, Whitney, Marsden, Douglass and many more. After a conference with Al Driscoll, back to New York for more meetings. To dine with Ernst Chain along with Roy and Mildred Grinker and then to see "Advise and Consent," a dramatic portrayal of the high points in the great novel by Allen Drury.

Dec. 9—To breakfast came Stanley Henwood for conferences on the volumes of the proceedings of the congress on congenital malformations and the conference on poliomyelitis. Visiting the bookstores and then to lunch at the Hemisphere Club, the new place at the top of the Time-Life Building. In the evening with Mark and Rose Soroko to dine at Lindy's and to see a wonderful musical comedy, "Tenderloin."

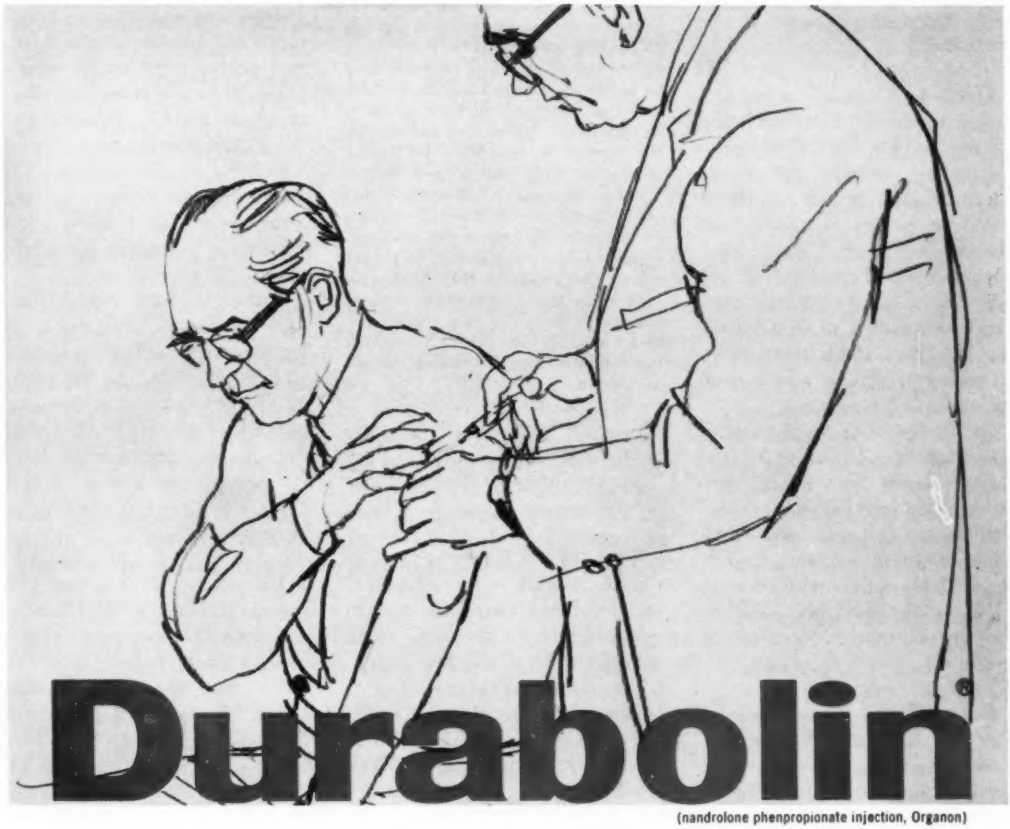
Dec. 10—With Ted Gotthelf and his lady to luncheon at the Four Seasons, where came also Paul Warwick with his staff. Then aboard a United Airlines DC-8 for Chicago.

Dec. 11—This day revising one of my books to bring it up to date, and it is amazing how many new important discoveries have been made in three years. Thereafter, reading Joe Sinclair's book "Anna Teller," a story of the Hungarian revolution and its effects on the *émigrés* in Detroit.

Dec. 12—Finishing most of the revisions of the book and began reading André Malraux' novel "The Metamorphosis of the Gods."

(Continued on page A-168)

in chronic fatigue and post-viral debility



Durabolin

(nandrolone phenpropionate injection, Organon)

once every 7 to 14 days provides safer, sustained anabolic revitalization

anabolic steroid	anabolic /androgenic	duration
Testosterone propionate (i.m.) Fluoxymesterone (oral)		3-4 days 1 day
Methyltestosterone (oral)		1 day
Norethandrolone (oral)		1 day
Durabolin (i.m.)		7-10 days

Chart adapted from Craig, P.: J. Okla. St. M.A. (June) 1960.

Green bar represents anabolic potency; gray bar shows relative androgenicity

Supplied:
5-cc. vials,
1-cc. ampuls (box of 3)
25 mg. nandrolone phenpropionate/cc.

Organon

Organon Inc.,
West Orange, N. J.

Dec. 13—This day came all the handicapped and disabled girls who are alumnae of the class which Mrs. Pepys conducted in the Spaulding School, and they were overjoyed with this celebration.

Dec. 14—Early came Dr. Novak to speak of a foundation for the Jackson Park Hospital to engage in research, and in the afternoon Mr. Segall to tell of the development of the Cancer Prevention Center. Then suddenly came news of the death of our dear friend, Meyer Kestnbaum, who was president of Hart Schaffner and Marx and a great leader in industry, public affairs and welfare.

In the evening to meet with the Board of Directors of the Dysautonomia Society, and encouraged a merger with other similar groups concerned with some of these genetic disturbances which individually affect so few but collectively bring sorrow and anguish to great numbers of families.

Dec. 15—In the evening to hear our orchestra led by Stokowski, and first they played a requiem for Kestnbaum. The orchestra then played Hungarian and Russian music so gorgeously that at the end the trumpet players gave the leader a fanfare.

Dec. 16—To dinner with Edmund Jacobson and his lady, and found here many of the faculty, including Percival Bailey and Joseph Kirsner.

Dec. 17—Now with the children under nine, which includes six of them, to Christmas parties at the Variety Club and the Standard Club. Thereafter to dine at the Hertwigs, along with Karl Meyer, the Hoffmans, the Friedells, Blaha, Mrs. Fritzell and Commissioner Duffy and his sister.

ALAS! POOR ENGLAND!

(From an address by William Ewart Gladstone in 1890)

"Another point upon which I congratulate the profession is its independence. It does not rely on endowment but on its own exertions directed to meeting human wants. There is no great profession which has so little to say to the public purse, and which so moderately and modestly dips its hand into the purse. It is not only in the interest of the public, but of the profession itself, that it is eminently self-supporting; and rely upon it, that the principle of self-support does much to maintain its honor and its independence, and to enable it to pursue its stately march in the times that have come and in the times that are coming, to form its own convictions, to act upon its own principles without fear or favor, for the general benefit of mankind."

* * *

Dec. 18—Early to hear Charles Angoff, critic and author and for many years assistant to my friend H. L. Mencken, speak with great wit of the Jewish contribution to literature. And it would seem that his special delight was Abraham Cahan's "The Rise of David Levinsky," which old Pepys read when it first appeared in 1917. He also mentioned particularly the writings of Ludwig Lewisohn, who sat at the *Stammtisch* in Schlögel's frequently in those old days.

Dec. 19—To the board of the Lyric Opera, finding that we have had a wonderful season and have even better prospects for the year to come, and reminisced with General Wood of the early days when Julius Rosenwald sent Donald Nelson to see old Pepys about removing the patent medicines from the Sears Roebuck catalog. In the afternoon and evening read "The Gentle Legions," by Richard Carter, a probing study of the national voluntary health organizations and of the United Funds.

Dec. 20—At noon to the Rotary Club for the annual Christmas party, enjoying the eggnog which Sidney Wanzer contributes regularly and also the singing of the Rotary Club Choir. Reading now "Welfare in America," by Vaughn Davis Bornet, a critical analysis of the United Funds versus the voluntary agencies.

Dec. 21—Now some 11 in. of snow on the ground and a zero temperature with it, so stayed indoors attending to the editing of the proceedings of the International Poliomyelitis Conference and reading, for the fun of it, one of the stories in John O'Hara's "Sermons and Soda Water."

Dec. 22—At the desk viewing great numbers of Christmas cards. In the evening to observe Margot Fonteyn dancing in "Ondine" with the Sadler's Wells Ballet. The legend itself is so delightful and so adapted to ballet for its expression that the evening was one of great enjoyment for all.

Dec. 24—With Judge Brown and his son and the Gerbers, he being the state insurance director, to dine at the Standard Club. Then all to observe the Sadler's Wells Ballet in "The Sleeping Beauty," which has the gorgeous music of Tchaikovsky, and the final act, "Aurora's Wedding," was one of the greatest of all ballet performances.

Dec. 25—Christmas Day with much cold and snow. The family came to dine, visitors arrived, and presents were exchanged.

And in bridge old Pepys, with Lester Marks as a partner, bid and made seven diamonds.

Dec. 26—Now comes the post-Christmas lethargy, and the children go to the Museum of Science and Industry enjoying most of all the birth of the baby chicks. And old Pepys began to dictate the letters of acknowledgment, which is a considerable task indeed.

Dec. 28—The children go to a production of "The Wizard of Oz" and old Pepys does magic with the DICTAPHONE®. In the evening to see "Giselle" danced by Margot Fonteyn and Michael Somes. Thought it well-nigh perfect, as did also my old classmate Dr. Louis D. Smith and his lady.

Dec. 29—To Indianapolis, arriving in the afternoon and meeting Samuel Mantel, and with him to the Marott Hotel. Then to the home of the Blochs, and here were many of our friends of younger days for a fine dinner.

"Willie dear," coaxed Mama, "say 'ah' so the nasty doctor can get his finger out of your mouth."

At a meeting of the American Society of Otolaryngologists, the chairman said: "All in favor of the motion say 'ah.'"

The king and the court jester were arguing over insults and apologies. The jester insisted that an apology may be worse than an insult. The king asked for proof. The jester fetched him a kick in the *derrière*. When the king turned angrily the jester said, "I beg pardon, Sire, I thought it was the queen."

* * *

Dec. 30—Lay late reading "The Waste Makers," by Vance Packard, which is full of insight regarding the American purchasing of unneeded objects merely to follow the legend created by promotion. Next to see the great warehouse of the J. P. Michael Company, which buys food for most of the hospitals and hotels of Indiana. In the afternoon to the home of A. Borinstein, whose family established the first home for aged persons in the city. In the evening to the country club for dinner and more mathematics.

Dec. 31—Reading now "Epidemic," by Frank Slaughter, who is a physician-novelist. He presumes an outbreak of plague in New York in 1965, while the city is making war against Communists. The fantasy is highly improbable and yet is told with enough knowledge of disease and delinquency to make a fascinating medical story. At night to dine at the Broadmoor Club and then again to the home of the Blochs for an evening of interesting amusement, and all greeted the New Year with the customary osculation and good wishes.

RICHARD ARMOUR

ALL SET TO GO

Broken bones, once they're properly set,
Don't argue, don't ask why or whether.
With little delay they get under way
And get busy getting together.

Rarely indeed do they balk and decline
And embarrass the patient and surgeon.
They're seldom the sort to sell anyone short
By sulking and failing to burgeon.

*

Broken bones mostly do what is right,
What is natural, proper and fitting.
Yes, it's lucky for all that after a fall
Or whatever, they tend to their knitting.

THE PERFECT NURSE

You doubtless know the nurse I mean:
She keeps things put away, and clean,
She's quiet, never makes a stir,
And loves the patients. (They love her.)

She comes to work a half-hour early,
Is always cheerful, never surly,
Works happily on holidays,
And never thinks about a raise.

She toils beyond the call of duty,
She's also got—well, she's a cutie—
The only trouble is, perforce,
She works for someone else, of course.

"...relief of itching...in some cases bordered on the dramatic."[1]